Ca

a Bulletin of

Cancer Progress

above and beyond the call of duty

Nearly 20 per cent of all cancers occur in the head and neck. About one half of these can be discovered by simple inspection and palpation. Tumors of the lips, gums, tongue, cheeks, soft and hard palates, jaws, face, ears, scalp, and neck, including thyroid—practically all tumors above the shoulder line, except the rare intracranial tumors—can be seen or felt by the physician who tries to find them.

The American custom of visiting the dentist twice a year makes thousands of patients available for examination for cancer of the mouth and lips. The dentist who is not content to limit his practice to tooth carpentry can give his patients an additional service far more valuable than the mere conventional dental work.

He has a wider stomatological viewpoint, observing the entire oral cavity. He looks for leukoplakia of the mucous membranes. He feels for abnormal swellings. He asks the patient about any open sores. And, above all, he follows through on any suspicion by arranging for confirmatory biopsy and insisting that the patient obtain immediate expert treatment. Life saving —the conventional province of the physician—thus becomes the basis of a citation of the dentist for unusual action "above and beyond the call of duty."

Cover—

INTERIOR LANDSCAPE, by Pavel Tchelitchew (1949). Painting in gouache from the Hugh J. Chisholm, Jr., Collection, Santa Barbara, California.

The transparent rendering of the human head reproduced in color on the cover is the work of the Russian-born American painter, P. Tchelitchew, who has earned fame and fortune with more opaque portrait heads of international socialites. The artist admits that he is producing neither exact anatomy nor fashionable portraiture, but he thinks he is reaching into something called "rhythmical time" and is on the way to depicting the fourth dimension.

This transparent topography is the outcome of a voluminous series of anatomical sketches in which the head, eye, ear, neck, and entire body were successively treated as x-ray views, which the creator calls "interior landscapes." Describing the anatomy as a "crystal jungle," he made the head and neck structures, superficial and deep, appear as lustrous and transparent as crystal. By the elimination, or rather the absorption, of many of the intricate interior distinctions and the creation of paths of light in concentric spirals, Tchelitchew gained a sense of wholeness and movement while seeing both the inside and the outside of the head at the same time. The head is enveloped in a series of spirals that encompass a strange galaxy of luminous bones. The blank spaces left between the light tracks establish a fluid rhythmical movement as an extra dimension added to the familiar three of breadth, height, and thickness. It is, in fact, "rhythmical time."

NEWSLETTER

JANUARY, 1956

Notes from ATOMS FOR PEACE Conference at Geneva (continued from the November, 1955, issue of CA)

Fateyeva gave this summary of Russian experience in the clinical and diagnostic application of isotopes: Radioiodine has been used for "a number of years" in Soviet clinics to determine the function of the thyroid gland. The absorption of radioiodine by the thyroid either increases or is at the highest margin of normal in more than 50 per cent of patients with stage-I hypertension; it decreases in stage III in 65 per cent of the cases, possibly because of secondary disorders in the blood. The rate of blood flow is determined with radioactive sodium. Hypertensive patients show a progressive retardation of blood flow. Blood flow is frequently accelerated in epilepsy, about normal in rheumatic heart.

Kozlova (Russia) gave this summary of the medical application of some radioisotopes: Radioactive cobalt, phosphorus, iodine, and gold are most widely used. Cobalt shows some advantages over radium and radiomesothorium as a radiation source in the treatment of some types of tumors; it is less damaging to normal tissues. Radioactive-cobalt treatment has been administered in the USSR "to a large number of patients" with malignant tumors of the skin, oral-cavity mucosa, tonsils, upper jaw, nasal cavity, larynx, esophagus, lungs, and breast, with metastases to lymph nodes and bones, as well as to patients with cancers of the genitalia. Of 450 patients with eyelid cancer treated in the Kharlov Institute of Roentgenology, 94 per cent recovered, and no complications were caused by the treatment. Treatment of gullet ring tumors with radiomesothorium produced favorable results in 61 per cent of the cases, while radioactive cobalt produced favorable results in 70 per cent of the cases.

Wallace (Cold Spring Harbor) stated that it seems unlikely -- barring wholesale exposure of populations to near-lethal doses of radiation -- that any reasonable level of exposure will result in the extinction of human populations. I personally doubt whether atomic disasters will

burden populations for thousands or even hundreds of generations with deleterious mutations; natural selection seems to act much too rapidly in eliminating semidominant, deleterious mutations. Genetic material passed on from generation to generation in irradiated drosophila populations gives rise to remarkably normal individuals.

Kemp (Denmark) reported that there is no doubt that the mutagenic effect of radiation on human beings will increase in the future, because mankind will be exposed to a larger dose of radiation than previously. The future development and genetic composition of a human population are dependent on a variety of factors, hereditary as well as environmental -- endogenous as well as exogenous. A very important group of these factors that determine the fate and survival of a race or a nation is composed of the hereditary deficiencies, abnormalities, and diseases occurring in the population. Beyond a definite intensity, further increase in radiation presents a potential hazard to the human race, as well as to plant and animal life. The most serious and effective precautions to control and prevent this risk and this danger have to be taken.

Carter (Medical Research Council, Harwell): In a civilized community the thesis is accepted that it is permissible to do harm to a few individuals when this is an unavoidable by-product of doing good to many. Airline passengers are still occasionally killed or injured, but nobody suggests that air travel should be banned. During the last year or two the public at large has become aware that even the peacetime use of nuclear power, with its benefit to the many, may entail danger to the few, and the public has become seriously disquieted by this realization. There is no agreement, even among the informed, about the exact nature and magnitude of the genetic danger from ionizing radiations, and there is no possibility of choice. In my opinion, we cannot today make any useful quantitative assessment of the genetic consequences of exposure of human populations to ionizing radiations at low dosage rates; we know far too little about human population structure and the induction of mutations in man. However, we know enough to be apprehensive about the genetic dangers. We now need a research program with three main parts: fundamental studies of mutation, studies of animal populations, and studies of human populations. Such a program would have

(Continued after page 36)

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CONTENTS

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Keeping up

TEM in Ovarian Cancer

On the basis of experience with triethylenemelamine (TEM) in twenty-six patients with advanced ovarian carcinoma, it is concluded that this therapy is indicated in nonresectable and recurrent ovarian cancers. TEM may be given before, after, or concurrently with roentgen-ray therapy. Of the twenty-six patients, fourteen were improved symptomatically, and in eight of these there was objective evidence of tumor regression. The usual duration of improvement was one to three months, but one patient was benefited for eleven months, and another, possibly owing to a spontaneous remission, still shows no evidence of recurrent disease after four years. The average survival period of the twelve patients not responding to TEM was five and one-half months. TEM was given either intravenously, in a daily dose of 0.04 mg. per Kg., or orally, one hour before breakfast with plain water, in a daily dose of 2.5 to 5.0 mg. for one or two days. Only an occasional patient treated intravenously complained of temporary anorexia, but about half of those treated orally complained of nausea, dizziness, or anorexia. The average course of oral therapy was 20 to 40 mg. TEM during the first month. Dosage was determined at one- to two-week intervals, on the basis of the patient's hematological and clinical response. If satisfactory improvement followed, maintenance doses were continued, under careful hematological control. Excessive dosage is indicated by severe leukopenia, thrombocytopenia, bleeding, and bone-marrow depression, the chief hazard of TEM therapy, which does not appear for two or three weeks after the last dose. Because of the insidious and relatively asymptomatic onset, the cure rate of ovarian cancer is not high. The five-year survival reported by Munnell and Taylor was 30.8 per cent. Hysterectomy, with bilateral salpingo-oophorectomy and removal of the entire carcinomatous process, is the treatment of choice. This was attempted when feasible in the twenty-six patients of this series, and twenty-four had roentgen-ray therapy after surgery. TEM offers a slight but definite advance in the palliative treatment of advanced ovarian carcinoma.

Sykes, M. P.; Rundles, R. W.; Pierce, V. K., and Kœrnofsky, D. A.: Triethylene melamine in the management of far advanced ovarian cancer. Surg., Gynec. & Obst. 101:133-140, Aug., 1955.

Treatment of Acute Leukemia

Management of acute leukemia varies with the age of the patient, cytological and clinical type, and severity of the disease. Although the results of treatment afford no grounds for optimism, they do show that the leukemic process can be checked for short intervals. Each physician must decide for himself whether to apply these officious attempts to induce remissions that are but ephemeral. By the treatment of acute leukemia, in addition to these slight benefits to the patient, advance has been made in the study of chemotherapy in cancer, since this form of cancer is so readily followed by objective tests. In rapidly advancing acute leukemia in children, therapy is begun with cortisone by mouth (up to 200 mg. daily), or with corticotropin by intravenous drip (25 to 40 mg. daily) or by intramuscular injection every six hours (100 mg. daily). Antimetabolites may be used concurrently

...with Cancer

but are better reserved for the first signs of relapse. Antimetabolites should be given in preference to cortisone and ACTH if the child appears to be likely to survive longer than three weeks; 6-mercaptopurine (2.5 mg. per Kg. body weight daily) is to be preferred to the folic acid antagonists, because its toxic effects are negligible. If 6-mercaptopurine does not produce a remission, one of the folic acid antagonists should be tried—aminopterin 0.5 to 1 mg. or amethopterin 2.5 to 5 mg. daily by mouth. By changing from one to another of these various specific measures, repeated remissions may be induced in favorable cases. In adults 6-mercaptopurine, 2.5 mg. per Kg. body weight daily, should be tried, combined with or followed by cortisone, 200 to 300 mg. daily. Blood transfusions alone induce satisfactory remissions in 15 to 20 per cent of patients. A hemoglobin level of 50 to 60 per cent should be maintained by transfusions while specific therapy is being given in an attempt to obtain remission. The general and local infections so common in leukemia are controlled by the usual antibiotics, preferably orally administered, since intramuscular injections commonly cause hemorrhage in the leukemic patient. The hemorrhagic state in leukemia is controlled only by transfusion of fresh blood. Thrombin solution is often effective in controlling gingival hemorrhage. In a six-year period at three London hospitals 121 patients with acute leukemia were treated with the several measures described. Partial remissions were obtained with folic acid antagonists in two of three children with myeloblastic leukemia and in two of six with lymphoblastic leukemia; one of two adults with monocytic leukemia had a short incomplete remission. With 6-mercaptopurine one child with myeloblastic leukemia had a good remission, but four adults showed no improvement; one adult with lymphoblastic leukemia had good remission and one of two children a moderate remission; two adults with monocytic leukemia had no remission. Cortisone or corticotropin gave the following results: myeloblastic—six adults (one complete, one partial remission), four children (one complete, two partial remissions); lymphoblastic—five adults (three complete remissions), five children (two complete, one partial remission); monocytic—three adults (no remissions). These few short-period remissions give hope that a means for controlling this tragic disease may some day be found.

Scott, R. B.: The treatment of acute leukaemia. Brit. M. J. 2:75-77, July 9, 1955.

Hodgkin's Disease

The first sign of Hodgkin's disease is frequently a cervical lymph-node enlargement that persists for three weeks or more. When a regional inflammatory lesion cannot be found to account for the enlargement, biopsy should be done. Even though the watchword in handling cancer today is "early diagnosis," which means histological confirmation of the clinical diagnosis, the question of performing a biopsy in a given case is often handled with indecision and delay. At times, it is difficult to establish a diagnosis, since the adenopathy may regress temporarily with antibiotic therapy or the biopsy may be misinterpreted. Re-examination at least every three months will eliminate overlooking

early stages of the disease. The clinical classification of Hodgkin's disease (employed in this series) should be noted at the initial examination: stage I: involvement of a single lymph-node group or organ, without constitutional symptoms; stage II: involvement of two adjacent lymph-node groups or of a single organ and regional lymph nodes, with or without constitutional symptoms; stage III: involvement of two separated lymph-node groups or of more than one organ, with constitutional symptoms. The primary treatment of Hodgkin's disease is roentgen-ray therapy.

With stage-I lesions, the entire group of involved nodes is irradiated through a large field. If the bowel or stomach is involved, the organ and adjacent nodes may be irradiated or the organ may be excised. With stage-II lesions, the involved areas and the adjacent group of lymph nodes are irradiated, while with stage-III cases all the involved groups of nodes are treated. The latter may require several series of treatments, with interposed rest periods. For patients with large, deep-seated lesions in the thorax or abdomen, supervoltage roentgen-ray radiation is employed to reduce the number of treatments. The over-all five-year–survival rate in a series of 216 patients was 37 per cent; the ten-year rate was 6 per cent. With stage-I lesions, the five- and ten-year–survival rates were 50 and 12 per cent respectively.

Healy, R. J.; Amory, H. I., and Friedman, M.: Hodgkin's disease; a review of two hundred and sixteen cases. Radiology 64:51-55, Jan., 1955.

Localization of Brain Tumors

The use of radioactive isotopes, with differential uptakes by normal and neoplastic tissues, to determine the site of brain tumors is a valuable adjunct to other methods of localization, ventriculography and angiography, especially when the tumor is in the lateral portion of the cerebral hemispheres. This method is of no value in localizing posterior-fossa or midline tumors. Gamma radiation from radioactive iodine capable of penetrating the intact skull is used to determine the site of the lesion before turning the bone flap. Beta rays from radioactive phosphorus, with soft-tissue penetration of but a few millimeters, are of value in more precise determination of tumor location after the skull is opened. To maintain the radioactivity of iodine for longer periods it is combined with human serum albumin. By the use of scintillation rather than Geiger counters the time required for an adequate test has been reduced from two or three hours to forty-five minutes. Of a group of thirty-nine cerebral-hemisphere tumors 61 per cent were correctly located by this technique. In nineteen of these the focal radioactivity of the tumors was 24 or more per cent greater than that of the surrounding normal tissue and all were correctly localized. Of fifteen expanding intracranial lesions all but one (an abscess) were correctly localized at operation with the needle probe using radioactive phosphorus.

Amyes, E. W.; Deeb, P. H.; Vogel, P. J., and Adams, R. M.: Determining the site of brain tumors; the use of radioactive iodine and phosphorus. California Med. 82: 167-170, March, 1955.

Au^{198} in Prostatic Cancer

Prostatic carcinoma was found by six pathologists in 14 to 46 per cent of men more than 50 years of age. Cancer of the prostate is the most common malignant tumor in men after 60, probably occurring in 20 per cent of all men past that age. Simple rectal examination is the most valuable single diagnostic means of detecting cancer of the prostate. When the tumor is confined to the capsule of the gland, total prostatectomy with removal of the seminal vesicles gives the best chance of cure. Estrogen therapy has contributed little to the survival time of patients with inoperable cancer of the prostate. Results reported by Flocks on more than 200 patients treated by interstitial Au^{198} justify extension and further study of this therapy. Au^{198} has a half-life of 2.7 days, its proportion of gamma to beta rays is favorable, and its production cost is relatively low. The present series consisted of twenty-six consecutive cases of advanced

carcinoma of the prostate, in many of which estrogen therapy had failed or the carcinoma had been reactivated. The four deaths in the series occurred in the first six cases, and serious complications arose only in the first ten patients treated. Serious complications are now practically nonexistent. Fourteen patients showed excellent results; three, fair; and two, poor. The ages of the patients were from 52 to 81, the average being 68.8 years. The average dose was about 2 mc. per gm. of estimated prostatic weight, which averaged 32 gm. Instillation was made retropubically and perineally. Five to 7 cc. of the gold solution may be injected through the perineum through a spinal needle with no ill effects.

Orr, L. M.; Campbell, J. L., and Thomley, M. W.: Treatment of inoperable prostatic carcinoma by Au[198]. J. Urol. 73:1089-1095, June, 1955.

Radiation Therapy in Management of Intrinsic Tumors of the Spinal Cord

Intrinsic tumors of the spinal cord arise from neuronal-tissue glial cells, vascular structures, and occasionally from other cellular components of the spinal medulla. Tumors that arise from the meninges and nerve-root sheaths or that result from the developmental inclusion of foreign dermal, fibrous, or adipose tissue within the substance of the spinal cord are not truly intrinsic tumors. The sixty-two cases analyzed (thirty-three men and twenty-nine women) consisted of thirty-nine pathologically classified tumors and twenty-three in which the diagnosis was established only by surgical gross inspection without removal of tissue. Of the thirty-nine histologically classified tumors, about two thirds were ependymona and one third were astrocytoma, while four patients had miscellaneous tumors, two of which were lipomas. Radiation therapy was administered to each of the sixty-two patients during the immediate postoperative period. The quality of radiation varied from a half-value layer of 0.95 to 1.2 mm. Cu, which is approximately equivalent to 200 kv. radiation with 1 mm. Cu and 1 mm. Al added filtration. The target-skin distance was 50 cm. The quantity of radiation delivered at each sitting, in the majority of instances, was 200 r as measured in air. The tumor dose per series of sittings ranged from 850 to 3950 r, and, while a number of patients received only one series (particularly those given 3000 r or more per series), some received as many as eight or nine and even fifteen series over periods up to fifteen years. It was found that the average survival is greater when immediate postoperative radiation therapy is administered than with surgery alone. Radiation therapy enhances recovery of function after surgical treatment and usually inhibits advancement of disability if recurrence takes place. Pain is almost always alleviated. Experience has produced a trend to conservative surgery, which usually consists of decompression by laminectomy, evacuation of areas of cystic degeneration in the case of intramedullary tumors, and removal of easily accessible portions of tumor in the case of lesions of the lumbosacral area. A trend exists, also, toward more intensive radiation therapy, although the value of higher dosage is not yet clear. Radiation therapy should be given to all patients with primary intrinsic spinal-cord tumors after surgical verification of the lesion.

Wood, E. H.; Berne, A. S., and Taveras, J. M.: The value of radiation therapy in the management of intrinsic tumors of the spinal cord. Radiology 63:11-23; disc. 23-24, July, 1954.

Lung Cancer

The suspected etiological factors in lung cancer are inhalation of tobacco smoke, radioactive dusts, and products of gasoline combustion. Ninety per cent of lung cancers occur in males, and 90 per cent in individuals between 40 and 70 years of age. Of the 658 cases diagnosed as primary pulmonary cancer at New York Hospital, 1932 to 1952, 401 (61 per cent) had positive microscopic diagnosis. There were 301 known deaths among these 401 patients. The classification of the 401 neoplasms was as follows: epidermoid carcinoma, 42 per cent; anaplastic carcinoma (including round- and oat-cell types), 37 per cent; adenocarcinoma, 14 per cent;

adenoma, 2 per cent; and bronchiolar carcinoma, fibrosarcoma, and chondrosarcoma, 2 per cent. Cough was present in 63 per cent, chest pain in 62 per cent, hypertrophic osteoarthropathy in 10 per cent, and superior vena-caval syndrome in 2 per cent. Of the 401 patients 181 had positive evidence of metastases at initial examination, operation, or autopsy. In order of frequency, metastases occurred in tracheobronchial and hilar lymph nodes, abdominal nodes, liver, ribs, adrenal, pleura, kidney, vertebrae, lungs, brain, pericardium, cervical lymph nodes, and numerous others. The treatment of choice was radical pneumonectomy—excision of the lung in continuity with its regional lymph nodes located in the hilar and mediastinal areas. One inoperable patient lived nine and another seven years with roentgen-ray treatment. Lobectomy in a few selected cases gave much better long-term survival than pneumonectomy. Among the patients in whom all gross tumor was removed and who left the hospital, the three-year–survival rate was 40 per cent; five-year, 40 per cent; and ten-year, 40 per cent.

Moore, S. W., and Cole, D. R.: Primary malignant neoplasms of the lung. Ann. Surg. 141:457-468, April, 1955.

Brain Tumor and Lumbar Puncture

The findings are reviewed in a series of 401 patients with histologically verified brain tumors in whom a lumbar puncture was performed. Fourteen per cent of the lesions were in the temporal lobe and 18.5 per cent in the posterior fossa. The 401 patients had a total of 447 lumbar punctures, but only one patient showed evidence of untoward reaction from spinal puncture. Lumbar puncture was useful in establishing the diagnosis of neoplasm in a large percentage of the cases. In 100 cases (25 per cent) the diagnosis of neoplasm was substantiated by an elevated cerebrospinal-fluid pressure, even though the optic discs showed no obvious papilledema. Papilledema (32 per cent) and increased cerebrospinal-fluid pressure (32 per cent) were present in a significant percentage of the cases. It is emphasized that this is a selected group of patients, since spinal puncture is not performed routinely in cases of brain tumor but is used chiefly to aid in the diagnosis in questionable cases.

Lubic, L. G., and Marotta, J. T.: Brain tumor and lumbar puncture. Arch. Neurol. & Psychiat. 72: 568-572, Nov., 1954.

Simple Mastectomy for Carcinoma

Simple mastectomy is without exception a palliative procedure. In a twenty-two-year period at Vanderbilt University Hospital sixty-one patients with carcinoma of the breast were treated by simple mastectomy, because the neoplasm had progressed so far as to be considered incurable, because of the advanced age of the patient, or because of some concurrent debilitating disease, with extremely poor general physical condition of the patient. Radical mastectomy was preferred in all cases in which the carcinoma was thought to be within the confines of the block dissection, regardless of the nature of the primary lesion or axillary metastases. Twenty (33 per cent) of the sixty-one patients treated by simple mastectomy survived more than five years. Thirty-eight per cent of patients without demonstrated distant spread and 77 per cent of those without clinically demonstrable axillary metastases survived five or more years. Palliation in the form of prevention of ulceration was obtained in those individuals with metastases. Biopsy of the internal mammary chain should be performed before deciding upon a radical mastectomy. If this biopsy shows carcinoma, simple mastectomy is to be preferred to radical mastectomy, since the latter also becomes a palliative measure only. Radiation is substituted for surgical treatment of the axilla.

Byrd, B. F., Jr., and Conerly, D. B., Jr.: The role of simple mastectomy in treatment of carcinoma of the breast. Ann. Surg. 141:477-481, April, 1955.

Ocular Evidence of Brain Tumors

Ocular signs and symptoms of 100 brain-tumor patients at Wills Eye Hospital, Philadelphia, are presented. Papille-

dema was present in 42 per cent and optic atrophy in 58 per cent. Headaches were present in 94 per cent and diplopia in 17 per cent. Visual-field defects were found in 69 per cent. Investigation of the endocrine status, of the integrity of other cranial nerves, and of the nasopharynx may yield evidence of a brain tumor and indicate the direction of further study. Tumor types in this series were: pituitary adenomas, 2.4 per cent; meningioma, 21 per cent; glioma, 18 per cent; metastatic tumors, 12 per cent; acoustic neuroma, 8 per cent; and craniopharyngioma, 5 per cent. Except for the gliomas and the metastatic tumors, most of these brain tumors were benign and amenable to surgical therapy. Even though the incidence of glioma is low, the malignant nature of this tumor makes early diagnosis important in patients with ocular complaints.

O'Rourke, J. F., and Schlezinger, N. S.: Evaluation of ocular signs and symptoms in verified brain tumors. J. A. M. A. 157: 695-700, Feb. 26, 1955.

Cancer of the Colon

Analysis of 750 consecutive cases of cancer of the colon, rectum, and anus at Jefferson Medical Center, Philadelphia, resulted in the following conclusions. The age extremes were 16 and 92 years; 61 per cent of the patients were between 50 and 70. Change of bowel habit was one of the earliest symptoms and occurred in 70 per cent of this series. Weight loss and anemia were more common in cancer of the right than in cancer of the left colon, and obstructive phenomena more common in cancer of the left colon. One half of all these cancers of the colon, rectum, and anus were palpable on digital rectal examination. Seventy-seven per cent of the lesions occurred in the lower sigmoid, rectosigmoid, and rectum, and three quarters of these were palpable rectally. Sixteen per cent of the patients had polyps of the colon, and 4 per cent had another colonic cancer, emphasizing the probable role of polyps as precursors of cancer of the colon. The assumption that rectal bleeding was due to hemorrhoids was the most significant cause for delay in diagnosis, and change in bowel habit frequently caused no immediate concern to the patient or the physician. The highest morbidity was caused by urinary-tract infection and the highest mortality by renal failure.

Follow-up on 93.6 per cent of the patients revealed an over-all five-year survival of 33 per cent, with 94 per cent of these clinically free of cancer. Of the rectosigmoidal and rectal group who were without evidence of spread, seventy survived five years.

Shallow, T. A.; Wagner, F. B., and Colcher, R. E.: Clinical evaluation of 750 patients with colon cancer; diagnostic survey and follow-up covering a fifteen-year period. Ann. Surg. 142:164-175, Aug., 1955.

Reconstruction after Surgery for Tumors about the Face, Head, and Neck

These conditions fall into the field of plastic surgery naturally because of the difficult problems of reconstruction, and many reports of these lesions come from this field of work. Plastic surgeons have been thought of as perhaps over-energetic in getting tumor areas closed, but they also know that many of the areas involved actually do better left open to reconstitute their own defects as far as possible naturally, to be followed by secondary reconstruction. This also gives more time for observation of recurrence of the growth, as may happen right through a laboriously reconstructed area if the removal procedure has not been done outside of the tumor field.

Brown, J. B.: A summary of development in plastic surgery from 1905 to 1955. Internat. Abstr. Surg. 101: 209-236, Sept., 1955; p. 231.

a glance . . .

one-minute abstracts of the current literature on cancer . . .

Cancer and the Dentist

The 90,000 dentists in the United States can contribute substantially toward the control of cancer. The periodic dental examination is more popular than the periodic medical examination. Almost everyone visits a dentist sooner or later. Since 12 to 15 per cent of all primary malignant lesions occur in the head and neck, the dentist is in a good position for early detection of a considerable number of cancers. Eighty per cent of deaths from cancers of the head and neck can be averted by early detection and adequate treatment. Many cancers of the head and neck are missed by the dentist because examination is confined to a mirror-explorer survey of the teeth and periodontium. History taking should be a more general practice among dentists. Is the patient hoarse? Is there a lesion of the skin about the face or ears? Is the face asymmetrical? Is there a swelling of the neck? In addition to roentgenograms, study casts, percussion, pulp tests, and transillumination as diagnostic aids, simple palpation, often overlooked, is most important. Any lesion that does not heal within two weeks may be cancer and indicates biopsy, the technique of which is far simpler than ordinary tooth extraction or gingivectomy and of negligible risk to the patient compared with that of postponement. When biopsy confirms the suspicion of cancer, the dentist is responsible for referral of the patient to a qualified surgeon and for making sure that treatment is not delayed. After operation, in conference with the surgeon, he provides the necessary rehabilitating prosthetic reconstruction.

Sandler, H. C.: The role of the dentist in cancer control. New York State Dent. J. 21:241-247, June-July, 1955.

Cancer of the Thyroid

All thyroid tumors should be excised for histological examination. Thyroid cancer occurs today three times as often as twenty years ago. All hope is denied the patient whose physician awaits the appearance of symptoms and signs—dyspnea, cough, choking, dysphagia, malaise, weight loss, anorexia, enlarged cervical lymph nodes, and fixation, hardness, and irregularity of the tumor. Of 833 patients at Albany Hospital with nodular goiter, 5.8 per cent were shown by the pathologist to have malignant diseases of the thyroid. Nearly half of the thyroid tumors in children are malignant. Removal of all thyroid lumps is advised. Lobectomy is carried out if the lesion is confined to one

lobe. Subtotal excision is done in the presence of multinodular, bilateral goiter and total thyroidectomy when no normal thyroid tissue is evident. As in cancer of other sites, surgery is designed to eliminate the tumor with its primary organ and all surgically accessible avenues of approach. In the case of thyroid cancer the entire lymph drainage, including the often neglected mediastinal portion, must be included. Three of four patients were found to have metastases in lymph nodes inaccessible from the cervical approach alone. Total thyroidectomy and examination of the tumor for type determination should precede treatment of metastatic foci with radioactive iodine. Roentgen-ray therapy is disappointing, as it is impossible to deliver a cancerocidal dose to the tumor without irreparable damage to normal tissues. Hormonal therapy has been of no value, and the value of chemotherapeutic agents is still undetermined. Tracheostomy as a palliative measure usually causes more, rather than less, distress. There comes a time in cancer therapy when it is a kindness to forget therapeutic possibilities and resort to comforting drugs. When the only remaining cancer is in the trachea or larynx, laryngectomy or removal of a part of the tracheal or esophageal wall is probably justifiable. These procedures yielded an over-all 57.5 per cent five-year–cure rate, 73.8 per cent for those patients with tumors of a predominantly papillary type, 70.2 per cent for the alveolar and follicular types, and but 3.8 per cent for the highly malignant type.

McClintock, J. C.: The treatment of thyroid cancer. New York State J. Med. 55:2376-2378, Aug. 15, 1955.

Treatment of Cancer of the Tongue

The preferred treatment of cancer of the tongue is surgical and includes radical neck dissection, with or without removal of the mandible, depending upon the extent of the primary lesion and the proximity of the closest metastases. The more radical the surgery, the better the hope of survival. The mandible must be sacrificed if the primary lesion closely approximates or invades the bone or if involved submaxillary nodes are closely applied to the bone. The recommended operative procedure is a one-stage, en bloc resection of the primary lesion and the entire field of lymphatic spread. Radiotherapy should be reserved for the inoperable and recurrent cases. The primary lesion may frequently be controlled by expert use of radium needles and radon seeds, but this therapy is quite ineffective in eradicating the metastases in the cervical lymph nodes that occur as frequently with cancer of the tongue as do metastases to the axillary lymph nodes with cancer of the breast, and radical surgery is preferred in both.

Freund, H. R.: Treatment of carcinoma of the tongue. New York State Dent. J. 21:252-256, June-July, 1955.

Differential Diagnosis of Oral Cancer

Careful distinction must be made between malignant and nonmalignant lesions of the mouth, lest the former be neglected or the latter lead to unnecessary mutilation of the patient. All lesions should be considered guilty until proved innocent, but no lesion should be treated as malignant before there is confirmatory roentgenological and laboratory evidence, particularly biopsy. Knowledge of the life history of the diseases is necessary in conjunction with the biopsy and other diagnostic procedures. For example, the rather common mixed tumor of the salivary glands is circumscribed and histologically benign initially but, if not completely removed, it recurs and often becomes malignant. Again, most benign tumors of the jaw in the young, such as juvenile ostotic dysplasia and myxomas, regress spontaneously after puberty, while others become circumscribed and can then be enucleated safely. The several forms of leukoplakia—lichen planus, leukokeratosis, and dyskeratosis—should all be examined histologically. Dyskeratosis is potentially malignant—carcinoma in situ—and should be ablated. In all cases of leukoplakia the cause should be eliminated and the patient kept under periodic surveillance. When

the common mouth ulcer does not disappear in a reasonable time, it should be biopsied. The causes of traumatic ulcers should be eliminated. Full-blown periadenitis mucosa necrotica recurrens, although benign, may resemble neoplastic ulcer. Concurrent lesions of the skin will usually identify oral ulcers of psoriasis, erythema multiforme, and lupus erythematosus. Biopsy is usually necessary in tumors of the bones. For example, benign eosinophilic granuloma in bone may simulate sarcoma clinically; only by microscopic examination can the diagnosis be made.

Cahn, L. R.: Differential diagnosis of oral cancer. New York State Dent. J. 21:248-252, June-July, 1955.

I^{131} in Thyroid Carcinoma

Forty-eight patients with carcinoma of the thyroid were investigated at the Royal Cancer Hospital. Tracer studies were made with 0.1 to 1.0 mc. I^{131} as sodium iodide. The amounts retained in the body and excreted in the urine were measured for several days. The thyroid and regions of suspected metastases were scanned, first with a Geiger counter, later with a scintillation counter, and recently with an automatic scanning apparatus. Thirteen of the forty-eight patients showed iodine uptake on the initial tracer study adequate to warrant I^{131} therapy. Twelve of these received 100 to 150 mc. Eight weeks later further studies were made, and additional amounts were given as long as there was evidence of adequate uptake. The maximum single dose was 230 mc., and the maximum total amount was 627 mc. over sixteen months. There was no marked depression of bone-marrow activity. Five of these eleven patients died shortly after therapy. Two have sustained improvement; one with remote metastases is alive five years after treatment. Only about 10 per cent of patients with thyroid cancer respond to I^{131} therapy, but there are occasional dramatic responses, as in a patient in this series with generalized pulmonary metastases who showed complete regression of demonstrable disease. Iodine studies with scanning devices have demonstrated metastases previously undetected by routine clinical methods, including roentgenography.

Kramer, S.; Concannon, J. P.; Evans, H. D., and Clark, G. M.: Thyroid carcinoma; a report on the diagnostic and therapeutic use of radio-iodine. Brit. J. Radiol. 28:307-313, June, 1955.

Oral Cancer

Controversy concerning choice of treatment of oral cancer has given way to cooperation between the radiologist and the surgeon. The dentist and the internist together with the surgeon and the radiotherapist constitute an effective team against cancer of the mouth. About 90 per cent of oral cancers are of the squamous-cell type originating in the mucous membrane. The remaining malignant tumors are adenocarcinomas, mixed tumors, lymphosarcomas, melanomas, etc. Tumors located anteriorly in the oral cavity are likely to be less malignant than those located posteriorly. Combined surgery and irradiation is often the most effective therapy, as in palate lesions and those posteriorly located. Small lesions of the lip are usually successfully treated by V excision. Larger lesions and those with lymph-node involvement require neck dissection and the necessary reconstructive surgery. Similarly, small and localized lesions of the tongue may be removed by adequately wide V excision, and longer lesions may require hemiglossectomy with neck dissection, a combination of surgery and radiotherapy, or radium-needle implants. Repeated biopsies may be required for diagnosis of palatal cancer, which is best treated by surgical or electrosurgical removal followed by intraoral cone and external portal irradiation. Wearing of dental prostheses should be delayed to prevent traumatic tissue necrosis, and the use of tobacco should be discouraged. In cancer of the buccal mucosa excellent results may be obtained by extensive surgery removing the necessary portions of the mandible, soft palate, anterior tonsillar pillar, tonsil, tongue, and lymph nodes of the neck.

Bogdasarian, R. M.: Treatment of oral cancer. New York State J. Med. 55:2213-2215, Aug. 1, 1955.

Urethane and TEM in Nasopharyngeal Cancer

At the Civil General Hopital, Singapore, thirty patients with nasopharyngeal cancer were treated with urethane and seven with triethylenemelamine (TEM). Twelve of the sixteen patients who completed full courses of urethane treatment were temporarily improved, and four did not respond. The tumors were more differentiated after than before urethane therapy. Urethane therapy combined with radiotherapy did not give better results than radiotherapy alone. Urethane therapy did not prolong life beyond the average thirteen months for these patients. The therapeutic and toxic doses of urethane approximate each other very closely. Anorexia, nausea, and vomiting were the most usual side effects. Urethane as a palliative agent may be considered when radiotherapy is not available and when the disease is too far advanced for radiotherapy. A maximum daily dose of 12 gm. of urethane for six days was given by intravenous drip with 2 pt. of 5 per cent dextrose solution. Of the seven patients treated with 2.5 mg. of TEM daily for four to six days, only one showed any response. There appears to be no indication for TEM in nasopharyngeal cancer.

Lawley, M., and Mekie, D. E. C.: Nasopharyngeal carcinoma. II. Treatment with urethane (ethyl carbamate) and triethylene melamine. Surg., Gynec. & Obst. 101:141-152, Aug., 1955.

Thyroid—an Anticarcinogen

Disturbance of the interior milieu of the body created by removal of one or more of the glands of internal secretion, or by prolonged administration of exogenous hormones, may cause cancer cells to grow and multiply more slowly or more rapidly, or even to be quiescent until they have adapted themselves to the new soil, and then to grow again. Thyroid hormone tends always toward restoration of normal endocrine balance. Hypothyroid states are frequently accompanied by growth of benign and malignant tumors of the breast and genitals. In the treatment of advanced cancer of the breast, thyroid administration should precede and follow oophorectomy and adrenalectomy, to retard the excessive production of the hypophyseal tropic hormones. When estrogens or androgens are employed in cases of advanced cancer, thyroid should be given concurrently, in order to spoil the soil for the recurrence of cancer. Thyroid hormone alone after radical cancer operations, as soon as the growth is removed, can prevent recurrences, even without deep roentgen-ray therapy. It is the thyroid hormone above all that restores a more normal metabolism unfavorable to cancer growth. Thyroid acts like an anticarcinogen.

[Loeser, A. A.]: Discussion on hormones and cancer. Proc. Roy. Soc. Med. 48:552-553, July, 1955.

Action of I^{131}

Ablation of the thyroid gland will follow a single, sufficiently large dose of I^{131}, but repeated doses are essential in the treatment of tumors, since the destruction of tumor tissue is uneven and patchy. The effect of I^{131} is to destroy zones of functional tissue, thus reducing the total volume of secretion, delaying the enlargement of a differentiated tumor or even reducing its size, and delaying bronchial obstruction and pressure on the spinal cord. Absence of early inflammatory reaction and hemorrhage, common to most other injuries, is probably due to the thrombosis and destruction of the blood vessels. In the rat, radionecrotic material appeared in the bronchi, which indicates a hazard (but not a great one) of cavitation, infection, and pulmonary collapse in treating pulmonary metastases with I^{131}. Surgery is not only not hampered but may be facilitated in some cases by the previous use of destructive doses of I^{131}.

Forbes, J. A.: The destructive effects of radioactive iodine. Brit. J. Radiol. 28:378-380, July, 1955.

Postoperative Oral Reconstruction

Difficult problems of reconstruction often arise as aftermaths of oral surgery for cancer. Small, early lesions without metastases and not involving bone leave

no closure problem, but extensive surgery and removal of important structures, such as the tongue and the mandible, often require long-term, complicated reconstructive methods. Small lesions confined to the lips can be simply excised and larger ones removed by V-excision, with closure. Mucous-membrane wounds heal promptly after close approximation of the raw edges. Full-thickness skin grafts are used in the correction of skin defects, but not in the oral cavity, where split skin grafts are used; these in time take on the appearance of mucous membrane. Intraoral grafts must be taken from surfaces without hair. The flap or tube graft brings viable soft tissue to any spot within the mouth, even deep within the oral cavity. The flap graft and tube graft, unlike the skin graft, carry subcutaneous tissue and their own vascularization and nutrition. Local flaps can easily be swung into position for correction of defects outside the mouth, but usually within the mouth grafts relayed over considerable distances are required. Tube grafts can be moved to the desired site end-over-end or they may be carried by one of the arms and, if necessary, can be utilized as a bed for future bone replacements.

Berry, E. P.: Methods of reconstruction following treatment of oral carcinoma. New York State Dent. J. 21:256-259, June-July, 1955.

Oral Biopsy

Formal biopsy is a comparatively simple procedure and is an essential part of the confirmation of the diagnosis of oral neoplasms. The diagnostic importance of the biopsy heavily outweighs the possible dangers of excessive hemorrhage, spreading of the lesion, and infection. Hemangiomas and other tumors of blood-vessel origin should be biopsied with great care. Suspected melanosarcomas are removed by wide excision, without cutting through the lesion. Bones are biopsied by the aspiration technique. Cautery, dyes (as local antiseptics), and serrated forceps should be avoided. The biopsy specimen should be deep and narrow rather than shallow and wide. Excision of tissue with a scalpel is the preferred method of biopsy of the oral cavity, since most lesions are readily accessible. Complete excision is justifiable only in cases of smaller lesions, and normal tissue should be included. Negative report on the first biopsy need not be accepted as final when the clinical factors suggest additional biopsies. The biopsy is important in determining the method of therapy, the extent of the surgical intervention, the degree of malignancy, and the probable degree of radiosensitivity. An unequivocal diagnosis of cancer of the oral cavity can be made only on the basis of the histopathological examination.

Kresberg, H., and Douglas, B. L.: Practical aspects of biopsy technic in the oral cavity. New York State Dent. J. 21:260-261, June-July, 1955.

I^{131} Radiation Sickness

Sickness after irradiation with radioiodine is qualitatively like that after a single exposure to medium-voltage roentgen rays—fatigue, headache, nausea, and vomiting. However, the latent periods are longer and the radiation doses lower in patients treated with radioiodine than in those given roentgen-ray therapy. The disturbance following a dose of radioiodine may occur in two phases, the first in four to thirteen hours (two to five hours for roentgen rays) and the second in five to nine days. Twenty-eight of thirty-eight patients treated with I^{131} showed symptoms of radiation sickness. Five patients were given I^{131} intravenously, and the others received it orally, after fasting, in activities from 29 to 200 mc. Incidence of radiation sickness and latent period were not influenced by the patient's general health but did vary with body size, as indicated by surface area calculated from the Du Bois tables, with dose rate, and with minimum dose.

Abbatt, J. D.; Court Brown, W. M., and Farran, H. E. A.: Radiation sickness in man following the administration of therapeutic radioiodine; relationship between latent period, dose-rate and body size. Brit. J. Radiol. 28:358-363, July, 1955.

Parotid Tumors

H. Mason Morfit, M.D.

All secretions within the oral cavity originate within the major or the minor salivary glands. The major salivary glands are three paired structures—parotid, submaxillary, and sublingual. Minor salivary glands are the small glands that line the oral cavity and upper respiratory passages. The histological structure of tumors arising from all of these sources is similar, and the site of origin of salivary-gland tumors must be determined upon clinical grounds. The parotid gland is far more commonly involved with tumor than the others. The submaxillary gland constitutes a poor second in frequency of involvement, with the minor salivary glands being third, and the sublingual gland only rarely being involved.

Frequency in Age and Sex

Parotid tumors (including malignant ones) can occur from birth onward throughout the entire life span. Hence, although the mean peak of occurrence is around 45 years of age for the benign tumors and approximately 55 years for the malignant tumors, the age factor itself cannot be used as a reliable guide in the recognition of these tumors. Large series usually show a slight preponderance of females over males, but, for practical purposes, the distribution between the two sexes is essentially equal.

Symptomatology

Benign parotid tumors nearly always present as painless, well-circumscribed masses on either side of the face, and in most instances no other symptoms can be elicited (Fig. 1). The parotid is a flat structure with irregular margins whose physical appearance and texture closely resemble those of the pancreas, and about 80 per cent of it lies superficial to the ascending ramus of the mandible. The remaining portion is retromandibular. Tumors may arise from any portion of the gland, but it is the superficial 80 per cent that is the seat of most of the growths, and for some reason, for which there is no adequate explanation, the "tail" is more frequently involved than any other area (Fig. 2). As the tumor increases in size, the characteristic external swelling appears. If the tumor arises from the retromandibular portion, the ascending mandibular ramus prevents external swelling, and the only visible evidence of tumor may consist of a bulge in the lateral pharyngeal wall (Fig. 3).

In benign tumors, the function of the facial nerve is never disturbed, this structure being pushed away by the advancing tumor margins at such a gradual pace that no dysfunction occurs. In contrast, malignant tumors will infiltrate the nerve, and the association of weakness or partial paralysis of the seventh nerve in conjunction with a parotid mass may be considered as strong evidence for cancer.

Differential Diagnosis

Infections of the parotid gland can be distinguished from tumors by the diffuse involvement, tenderness to palpation, and pain with mastication or ingestion of sour substances. An initially favorable response of these symptoms to antibiotics and heat, followed, in most instances, by a later exacerbation, is common. Precipitation of the minerals in the salivary secretions with stone formation occasionally occurs but is easily recognized in the roentgenogram. This is more common in the submaxillary gland.

Lymph nodes lie within the parotid

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gland but in the normal state are not palpable. An enlarged lymph node, however, can closely resemble a parotid tumor. These nodes drain the parietal and temporal areas and the skin around the eyelids (Fig. 4). Examination of these areas, therefore, for evidence of a skin cancer plus careful questioning concerning the removal of a mole or a skin cancer in the recent past should be a part of every ex-

FIGURE 1. Presenting appearance of some benign parotid tumors.

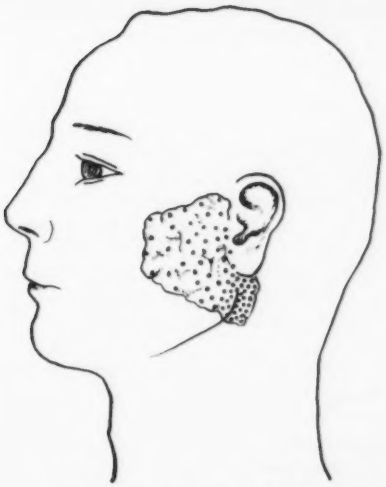

FIGURE 2. Scattergram of seventy-four cases of parotid tumors. Each dot represents one case. The "tail" is most frequently involved.

amination. As one checks these points, with negative results, the probability of the parotid enlargement being explained on such a basis lessens, and the chances of the mass being a primary parotid tumor becomes increasingly stronger.

Soft-part tumors (lipomas, fibromas, etc.) may develop in any part of the body and the parotid area is no exception. Their occurrence here is infrequent, however, and, since their treament is much the same as that for other parotid tumors, they have caused no difficulty. Very rarely, anomalies of the first branchial cleft may develop, but here again their treatment is essentially the same as that for a removal of a parotid tumor.

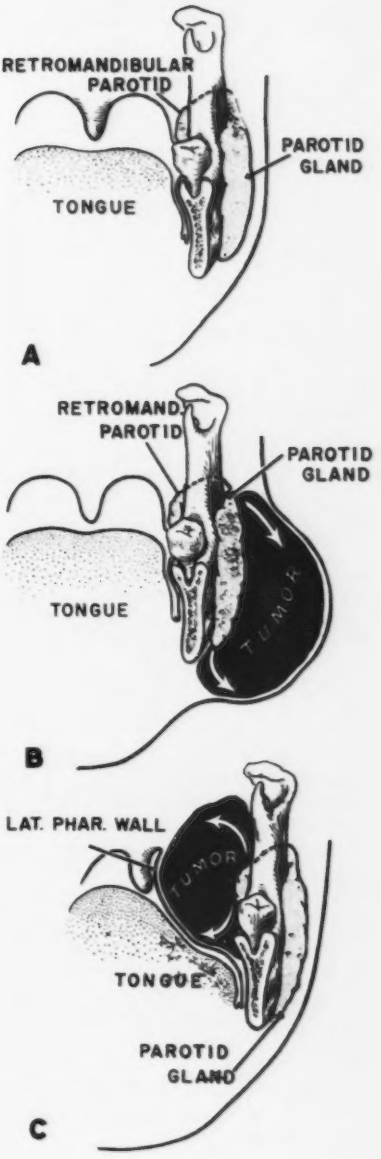

FIGURE 3. A, Although most of the parotid gland lies externally, a small portion lies posteriorly and medially to the ascending mandibular ramus. B, Most parotid tumors arise lateral to bone. As they increase in size, they produce classical external preauricular swelling. C, Tumors arising from the retromandibular portion expand medially owing to the unyielding lateral bony wall. No external mass appears and the only symptom is bulging of the lateral pharyngeal wall.

(For caption see opposite column.)

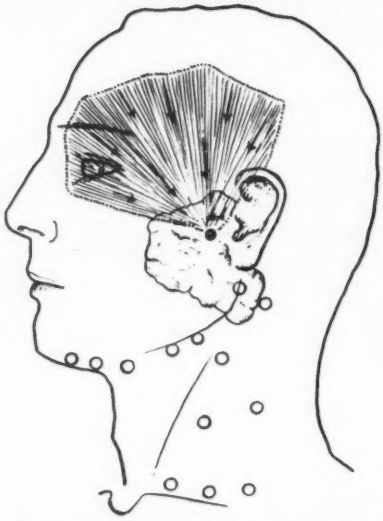

FIGURE 4. Location of the lymph nodes of the parotid and the neck. The shaded area drains to the parotid node and should be closely inspected for skin cancer, malignant melanoma, etc. that will metastasize here first and may simulate a primary parotid tumor.

Curiously enough, the mistaken diagnosis of a sebaceous cyst is one of the frequent errors made in these cases. Superficially, there is a resemblance between the two entities. A sebaceous cyst, however, arises from a skin appendage, and careful scrutiny will show it to be still attached to the skin. Frequently, with proper lighting a telltale pit in the skin, marking the retracted "pore" indicating the sebaceous gland that has become blocked, with resultant cyst formation, can be seen. In contrast, parotid tumors in the benign state or even in early cancer will have no connection with the skin and move freely about in the subcutaneous tissues. Sialograms have been employed by us but have been discarded as a diagnostic aid not worthy of the trouble and effort expended.

Clinical Course

THE MOST IMPORTANT THING TO REMEMBER CONCERNING THE CLINICAL COURSE OF PAROTID TUMORS IS THAT, DESPITE THEIR INNOCUOUS APPEARANCE, A SIGNIFICANT PROPORTION OF THEM ARE CANCEROUS AND THEREFORE HAVE THE CAPABILITY OF KILLING THE PATIENT UNLESS THEY ARE REMOVED. Furthermore, it is impossible by clinical examination alone to distinguish the benign tumors from malignant ones. Although the association of a parotid swelling with evidence of dysfunction of the seventh nerve can be considered pathognomonic of a cancerous tumor, the absence of such an association does not exclude this possibility and may only indicate that, up to this point, the tumor has not yet infiltrated the nerve. The incidence of malignancy in our series of cases (seventy-four patients) has been approximately 20 per cent.

It has now been established that the transition from a hitherto benign to a fully malignant tumor can occur at any time.[3, 4] Statements by patients, therefore, to the effect that the lesion "has been present for five, ten, fifteen, or more years and has never caused any trouble" cannot be relied upon as a guarantee that no such difficulty will develop. In one of our cases, the patient had had a parotid tumor for thirty-five years without its producing any serious disability. In the thirty-sixth year the tumor showed a marked exacerbation in growth, was removed, found to be malignant, and ultimately killed the patient within fifteen months.

Local recurrences after removal have been so notorious that some authors have taken the position that, if one waits long enough, this will develop in every case. It is certainly true that the traditional five-year waiting period for evaluation of results does not have the same significance here as it does in some other tumors, since difficulties have arisen ten or more years after the original treatment. A common explanation for these recurrences is the theory of multicentric origin. Studies by Foote and Frazell[3, 4] have provided a better explanation for this phenomenon. Grossly most of these tumors appear to be well encapsulated. The surgeon, being aware of the fact that he is in close proximity to the seventh nerve and having no

desire to damage it, has stayed too close to the capsule during its removal. Figure 5 shows that buds of tumor tissue extend within and beyond the capsule and that therefore any such plan of attack involving "shelling out the tumor" carries with it the probability of leaving behind such small nests of tumor cells, which will ultimately be the source of recurrences. The significance of this will be discussed further under treatment. Histological classifications and microscopic criteria for diagnosis have been described elsewhere[3, 5] and are not included here.

Treatment

Except in rare instances salivary-gland tumors do not respond well to radiation therapy, and the main reliance for their control must rest with surgery. The capricious behavior of the malignant tumors makes it very hard to lay down a black-and-white course of action for their treatment, beyond stating that a wide removal of the primary tumor is indicated. Metastases to the regional lymph nodes (the neck) do occur, but on the other hand a great many patients will die from distant dissemination to bone, lungs, brain, etc., and lymphogenous spread will not occur.

In my opinion these tumors constitute one of the few exceptions on which definitive therapy should be carried out without the benefit of a preoperative biopsy. Semisolid myxomatous tissue and marked cellularity frequently associated with cyst formation are common characteristics of these lesions. As long as the capsule is maintained intact, the surgeon has a fair opportunity to accomplish complete and successful removal. Biopsy, even with a needle, necessitates a breech be made in this capsule, and therefore the possibility of these soft, cellular elements gaining access to the adjacent tissue planes is a real one.

The clinical examination coupled with a careful history will permit a diagnosis to be made with a high degree of accuracy without the aid of corroborative biopsy. One should therefore approach this entity with the same concept that the surgeon

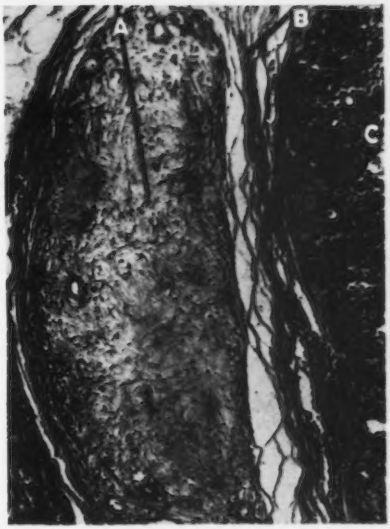

FIGURE 5. Photomicrograph showing the tumor extending into and beyond the tumor capsule. "Shelling out" the tumor exposes the patient to the risk of leaving these nests of cells behind and to the development of local recurrence. A, tumor cells extending into and beyond the capsule; B, capsule; C, main mass of tumor. (From Foote and Frazell: Tumors of the major salivary glands. *Cancer* 6: 1065-1133, 1953.)

approaches right lower-quadrant pain, where we know that the diagnosis of appendicitis will not always be correct, but the risks of withholding surgery exceed those associated with surgical exploration. In our seventy-four cases an inaccurate preoperative clinical diagnosis was made on only one occasion: the tumor proved to be a lipoma.

Experienced individuals now are in unanimous agreement that proper treatment requires that an attempt be made to remove the tumor together with a generous portion of surrounding apparently normal parotid gland. The technique for this has been described elsewhere,[2, 4, 6, 7] but basically it consists of identifying the seventh nerve at its point of emergence from the styloid foramen and removing all of the parotid gland superficial to the

(*Continued on page* 20)

COMMON FATAL DIA

From Inadequate Examina

"Hemorrhoids," for cancer masked by hemorrhoids

"Functional vaginal bleeding," for bleeding from cancer.

"Benign mole," for malignant melanoma

DIAGNOSTIC ERRORS

amination without Biopsy

"Canker sore," for oral cancer.

"Chronic mastitis," for breast cancer

"Prostatic hypertrophy," for prostatic cancer.

mandibular ramus. In benign tumors the nerve can be preserved and the patient recovers with normally functioning facial musculature. As the dissection proceeds, the nerve may be seen to run in close proximity to the tumor. In benign lesions the nerve can usually be dissected away; but, if the nerve does not come away easily and appears to be stuck to the tumor, the probability of the lesion being malignant is strong, and this portion of the nerve will be purposely sacrificed.

To attempt operative removal without exposing and dissecting out the seventh nerve greatly increases the chances both of incomplete removal of tumor and of damage to the nerve, and we consider this step to be a prime requisite in a successful operation. This operation should be selected as the initial step in treatment and not reserved for use in cases previously operated upon or in failures from other modes of treatment. A comparison in results with this approach as applied to "fresh" cases in contrast to those in which a previous operation or incision has been made shows a fall-off in the curability of approximately 17 per cent (Table 1). Unless the physician feels himself capable of following these principles, he does the patient a disservice to attempt treatment at all and would be wiser to refer the case to someone more familiar with the problem.

If cervical metastases are present, these should be dealt with by means of the classical neck dissection. The procedure, however, is reserved only for those patients with proved metastases and is not recommended as an elective or so-called prophylactic operation.

TABLE 1

End Results in 262 Benign Tumors of the Parotid*

Treatment	5-yr. cure, %
No previous surgery	95
Surgery prior to admission to Memorial Hospital	78

*From the Head and Neck Service, Memorial Hospital.

Case Histories Illustrating Common Errors in the Treatment of Parotid Tumors

Case 1. A 24-year-old, single, white woman applied to her physician with a painless 2-cm. swelling in front of the right ear. A clinical diagnosis of a sebaceous cyst was made and the patient was advised that the lesion could be removed as a simple office procedure. This was attempted and it became evident that the lesion was not a sebaceous cyst. The tumor was ruptured, spilling its contents into the small surgical wound, but this did permit the surgeon to obtain tissue upon which a correct diagnosis was subsequently made. The patient was ultimately referred for a more complete operative removal, but she had a reduced chance of a successful result (Table 1).

Case 2. A 42-year-old, single, white man has a correct clinical diagnosis of parotid tumor made, and the patient was advised to enter the hospital for operative removal. The surgeon believed that the tumor was superficial and could be removed by "shelling it out" without worrying about the nerve. However, the tumor extended more deeply than had been anticipated, and the surgeon ultimately felt it necessary to back out for fear of damaging the nerve in the course of removal, owing to the fact that he had not exposed and identified the nerve as a part of his operation. Paralysis of the upper facial muscles was present when the patient awakened. It was impossible to determine whether this branch of the nerve had actually been severed or whether it had been simply crushed or pinched (in which case ultimate recovery of function would have appeared). A second operation was necessary, during which the superficial portion of the gland containing the tumor was removed after the nerve had been exposed and identified, but the branch of the nerve going to the eyelids was found to have been severed at the initial operation.

Case 3. A 55-year-old, married, white woman with a preauricular swelling entered the hospital and had a formal biopsy made through the overlying skin

into the tumor mass. The lesion proved to be a cellular cancer and the cells spilled out into the adjacent tissues, resulting in a lessened possibility of a satisfactory result, despite a later more definitive operative removal. This could have been avoided if complete operative removal had been carried out as the first step even without the benefit of biopsy.

Case 4. A 48-year-old, married, white woman with the history of a parotid swelling for eight years had seen four different physicians during this time but had been advised by all of them "to do nothing unless it begins to bother you or increases in size." In the months prior to her last admission, the tumor began to show increased activity and, when removed, proved to be cancerous. Her history indicates that, at least during the early stages, the tumor was benign and only in recent months became malignant. Surgical removal was carried out along the lines described earlier, but, instead of a 95 per cent probability of a good result, which obtains if the lesion is benign, her chances of cure were considerably reduced by waiting until the same operation was carried out on a malignant tumor. ALL PAROTID TUMORS SHOULD BE REMOVED.

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KINESCOPE 17: HEAD AND NECK CANCER

HAYES MARTIN, M.D.
Attending Surgeon, Head and Neck Service
Memorial Center for Cancer and Allied Diseases
Associate Professor of Clinical Surgery
Cornell University Medical College

MEMBERS OF THE ATTENDING STAFF
Head and Neck Service
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APPROVED FOR INFORMAL STUDY CREDIT BY THE AMERICAN ACADEMY OF GENERAL PRACTICE

Carcinoma of the Thyroid Gland

Danely P. Slaughter, M.D.

The subject of carcinoma of the thyroid gland has created more of a controversy in the literature in recent years than its numerical incidence warrants. Actually, thyroid cancer is one of the less common forms of malignant neoplastic disease, as compared with cancer of the skin, breast, lung, uterine cervix, and gastrointestinal tract. However, the importance of the problem lies in the fact that, from this recent spate of published studies, a clinical pattern has evolved whereby one more form of major cancer can be recognized in an early, curable, and easily treatable stage. Furthermore, it is entirely possible that this pattern of clinical approach may add thyroid cancer to the list of those malignant tumors to which the emerging concept of true cancer prevention may be applicable.

Incidence of Thyroid Cancer

Diseases of the thyroid gland appear to be decreasing in frequency, with an accompanying shift in their pattern of incidence. Exophthalmic goiter occurs much less frequently than it did twenty years ago, and toxic nodular goiter seems likewise to be less common. Whether the incidence of nontoxic nodular goiter and of cancer of the thyroid is changing in either direction is not clear. The reported occurrence of thyroid cancer varies from 3 to 7 per cent of all surgically treated thyroid disease. If the various types of thyroid disease are evaluated separately, the incidence of thyroid cancer varies remarkably in relation to the clinical setting in which it occurs. For instance, in patients with exophthalmic goiter, cancer of the thyroid is almost nonexistent. In the 1945 publication by Cole, Slaughter, and Rossiter of a study of 1000 consecutive surgically treated thyroid patients, thirty-eight cancers were found, an incidence of 3.8 per cent. Approximately half of this material consisted of patients with exophthalmic goiter, in which only one instance of cancer was found, an incidental Hürthle-cell adenoma interpreted as being malignant. Therefore, practically all the cancers occurred in the other half of the thyroid cases, the nodular goiters, thus essentially doubling the cancer incidence in this group. In the group of toxic nodular goiters, the cancer incidence was only 1.2 per cent, thus implicating the nontoxic nodular goiter as the clinical setting in which cancer is most likely to be found.

From the Department of Surgery and the Tumor Clinic, University of Illinois College of Medicine and the Research & Educational Hospitals, Chicago, Illinois.

TABLE 1

Incidence of Thyroid Cancer in All Types of Goiter Removed by Operation at Illinois Research Hospital*

1936 to 1952 Inclusive

	1936 to 1944		1945 to 1952		Total: 1936 to 1952	
Type of goiter	No. of cases	Cancer %	No. of cases	Cancer %	Total no. of cases	Cancer %
Toxic diffuse	433	0.2	147	0	580	0.1
Toxic nodular	330	1.2	71	0	401	1.0
Nontoxic nodular						
Solitary	92	24.0	161	19.3	253	20.9
Multinodular	100	11.0	95	6.3	195	8.7
TOTAL	192	17.1	256	14.4	448	15.6
TOTAL	955	3.9	474	7.9	1429	5.2

*Data from Majarakis, Slaughter, and Cole.

TABLE 2

Incidence of Thyroid Cancer in Nontoxic Nodular Goiter*

Reports in the Literature

Author	Location	Year	Cancer in all nontoxic nodular goiters %	Cancer in solitary nontoxic nodular goiters %
Lahey & Hare	Boston	1951	5.9	10.0
Ward	San Francisco	1944	4.8	15.6
Young	Oklahoma	1950	9.4	18.2
Cope et al.	Boston	1949	10.1	19.0
Cerise et al.	New Orleans	1952	17.3	19.8
Hinton & Slattery	New York	1952	7.2	
Majarakis et al.	Chicago	1952	15.6	20.9
Crile[6]	Cleveland	1950	10.9	24.5
Beahrs et al.	Rochester, Minn.	1951	3.8	

*Data from Majarakis, Slaughter, and Cole.

This group was further broken down into the multinodular nontoxic goiters and the clinically solitary, unilateral, nontoxic masses in the thyroid. The incidence of cancer was, respectively, 11.0 per cent and 24 per cent and, in both combined, 17.1 per cent. These figures not only startled us but apparently had the same effect on other students of the problem throughout this country, particularly when the percentages were carelessly quoted out of context. These findings prompted reviews of the clinical thyroid material in many other centers, and two subsequent reviews of our own. Our own figures appear in Table 1 and those of others in Table 2.

It is apparent from these studies that cancer is present in at least 10 per cent of solitary, unilateral, nontoxic nodules in the thyroid gland. This percentage (Lahey) is the lowest quoted in Table 2, the others being so much higher that the true incidence in the country as a whole is undoubtedly greater. It would appear, therefore, that a clinical setting has been defined in which undiagnosable thyroid cancer may be found in a stage when it is very amenable to curative attempts and in such frequency that the law of diminishing returns does not apply to the effort expended to find and eradicate the disease. It is well known that the cure rate of thyroid cancer is much greater in those patients whose cancer had not been diagnosed before surgery.

Does Thyroid Cancer Require Treatment?

This seemingly silly question has been raised by some observers who are impressed with an occasional patient whose thyroid cancer pursues a very prolonged and sluggish course, even up to twenty-five years and more. The vagaries of the natural history of this disease make its course less predictable than that of most other uncontrolled cancers. Another difficulty is the uncertainty of precise microscopic definition of a few thyroid tumors. This doubtful group actually constitutes only a small fringe of the total of thyroid cancer and probably cancels itself out, in large series, by inclusion of a minute percentage of both false positives and false negatives.

Another factor leading to an amiable regard of thyroid cancer is the fortunate fact that the majority of these tumors are predominantly of the papillary type, the least aggressive and most easily curable of the malignant tumors of this organ. It is equally true that the rare giant- and spindle-cell type of thyroid cancer is virtually incurable.

Our experience at Illinois Research Hospital belies the equanimity with which some observers seem to regard thyroid cancer. Up to 1952 our 5-year–survival rate was 36.8 per cent,[16] within the range of some reported 5-year–cure rates of ma-

lignant melanoma or testicular tumors. In this 5-year–survival group are some patients with obvious active disease who are destined to die of thyroid cancer eventually, if a highway accident, coronary thrombosis, or some other fatal episode does not supervene. From the literature it is apparent that other opponents of thyroid cancer find it a difficult disease to control. Table 3 lists some published experiences from recent years, and it is suggested that the reader subtract the survival percentages from 100, to obtain a more accurate conception of what happens to people with cancer of the thyroid gland.

Diagnosis of Thyroid Cancer

Carcinoma of the thyroid appears in many guises but, as a simplification, three clinical states may be recognized:

The Clinically Evident Cancer. These are obvious because of local findings in the thyroid area. When a hard, fixed mass occurs, especially with vocal-cord paralysis and cervical lymph-node metastases, the diagnosis is practically certain. This clinical setting affords the lowest cure rate, next to that with distant metastatic spread.

The Suspected or Unsuspected Thyroid Cancer. This is the most important group because it furnishes the highest cure rate of all. One cannot separate the suspected cancer cases from the unsuspected group as clearly today, because the index of suspicion in all nontoxic nodular goiters is rising, particularly in the unilateral thyroid masses. In these groups the surgeon should have mental reservations about the possibility of cancer in practically every case. Furthermore, the surgeon should cut and examine all the thyroid tissue removed, while still at the operating table, and frozen section should be done on all suspicious tissue. Frozen-section diagnosis of thyroid tumors is not so difficult as it formerly was thought to be and, in fact, is quite accurate. Definition of a malignant lesion during the operation certainly gives the surgeon a better chance to extend his procedure in a curative attempt, than when the same information is received four or five days later. It has been demonstrated that the cure rate of these thyroid cancers that can be diagnosed with certainty only at the operating table is on the order of two to three times greater than that of the clinically evident cancers. This category of uncertain or unsuspected thyroid cancer assumes even greater importance from the fact that it now constitutes half or more of thyroid-cancer material, and this percentage appears to be increasing.

Distant Metastasis as First Sign. The occasional patient with a pathological fracture, brain involvement, or other evidence of distant metastatic disease demonstrates an unusual but distinct clinical pattern in thyroid cancer. These patients

TABLE 3

Five-Year–Survival Rates (Mean) in All Types of Thyroid Cancer*

Reports in the Literature

Author	Location	Year	No. of patients followed 5 yr.	Five-year survival (mean) %
Beahrs & Judd, Jr.	Rochester, Minn.	1951	284	71.5
Horn et al.	Philadelphia	1947	42	55.0
Frazell & Foote	New York	1950	215	39.1
MacFee	New York	1952	34	38.2
Majarakis et al.	Chicago	1952	49	36.8
Portmann	Cleveland	1940	149	35.5
De Quervain	Switzerland	1935	108	17.5
Dargent	Lyon, France	1941	135	9.6
Watson & Pool	New York	1940	167	7.8
TOTAL			1183	37.1

*Data from Majarakis, Slaughter, and Cole.

FIGURE 1. Unilateral mass in thyroid of many years' standing that had undergone some recent growth. This proved to be an operable carcinoma of the thyroid arising from a previous unilateral goiter.

usually have had a goiter of many years' standing, apparently unchanged and innocent. Diagnosis ordinarily is made by biopsy of the metastatic lesion, with the surprise finding of cancer of unmistakable thyroid origin. This is the group that might have been salvaged by surgical recognition of early cancer in the nontoxic nodular goiter years before, the course present teaching would indicate.

Vocal-cord paralysis is very rarely seen in benign goiter, but it must be emphasized that normal cord motility by no means rules out the presence of cancer. Less than half of the thyroid-cancer patients at Illinois Research Hospital had cord paresis. Another point of diagnostic importance is the fact that thyroid cancer is asymptomatic until the later stages, when hoarseness and airway obstruction will become a problem. These patients only very rarely have true hyperthyroidism. The disease occurs at a younger age than the average for other forms of cancer, and malignant tumors of the thyroid occur in children and teen-agers. Diagnosis, then, depends on physical examination, alertness, and suspicion, particularly in nontoxic nodular goiter, and especially when a clinically unilateral mass is present. Occasionally a primary lesion of the thyroid will be minute and impalpable, yet produce multiple neck node metastases. In such a situation excision of a node and identification of the tumor microscopically will show it to be of thyroid origin, usually papillary in character. Exploration of the homolateral thyroid lobe will ordinarily reveal the primary (Figs. 3, 4).

Treatment

The definitive treatment of thyroid cancer is surgical, radiation methods being only an important adjunct. The surgical approach should be so planned that biopsy of a thyroid tumor does not seed any of the operative field, should the lesion turn out to be malignant and operable. For this reason, in the unilateral thyroid masses it is our practice always to do a total lobectomy with dissection and preservation of the recurrent laryngeal nerve. If the lesion proves to be malignant, this avoids the dilemma of inadequate surgery and the decision whether to reoperate or to use radiation in the hope of eradicating cancer left behind. If a papillary type of cancer is found, and especially if metastatic

FIGURE 2. Inoperable and incurable carcinoma of the thyroid of mixed papillary and adenocarcinoma type. This tumor likewise arose from a pre-existing unilateral goiter of many years' standing.

disease in nodes is discovered, it is our feeling that a radical neck dissection should be done in most cases. This should include the inferior thyroid and upper mediastinal nodes, and, if these are involved, we do not hesitate to split the sternum for better access. We have not as yet adopted this latter procedure as a routine measure. The opposite lobe of the thyroid should always be explored because bilateral thyroid cancer is apparently much more frequent than was previously realized.

Roentgen-ray radiation is used as a postoperative measure only in the advanced and barely operable cases or for the inoperable ones in which cancer is known to remain. Here interstitial radiation, in the form of radon seeds, is the most effective method of radiation control. Radioactive iodine has not been of so much use as was at first hoped. Only about 15 per cent or less of thyroid cancers will pick it up in any effective concentration. A few more tumors can be made to take up I^{131} if all normal thyroid tissue is removed. This is of use in the patient with distant metastatic disease, e.g., in the femur or the spine, where there is no take-up. Occasionally one of these tumors will redifferentiate toward the normal after total thyroidectomy and will take up the I^{131}.

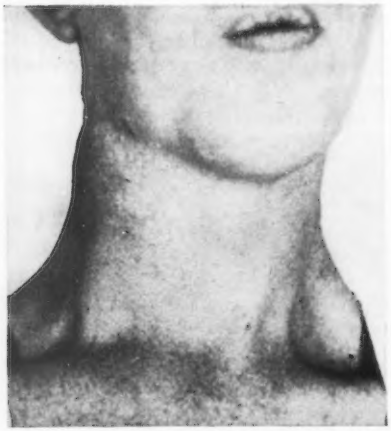

FIGURE 3. Mass in right upper neck that on biopsy proved to be papillary thyroid carcinoma metastatic from a minute focus in the upper pole of the homolateral lobe. On thyroidectomy and radical neck dissection, multiple nodes were found to be involved with metastatic disease, and a small, 5-mm., impalpable primary tumor was found in the thyroid gland itself. This is the clinical setting that formerly was referred to as lateral aberrant thyroid but that today is known to be metastatic disease from a minute primary lesion in the thyroid gland.

FIGURE 4. Tenth-day postoperative picture of a patient who had a right thyroid lobectomy and radical neck dissection for carcinoma of the thyroid gland with multiple node metastases. This patient has survived eleven years free of disease. The photograph illustrates the usual type of incision utilized for this operative procedure.

Summary

Malignant tumors of the thyroid gland are not common, but they are among the more easily curable of the major cancers. They can be found as unsuspected lesions in a curable state by exploring nodular nontoxic goiters and by performing lobectomy for unilateral or solitary adenomas, since the percentage incidence in these types of goiter is reported as from 10 to 24 per cent. Because many thyroid cancers are slow growing and pursue a course sometimes of years' duration, they should not be taken lightly, but, on the contrary, serious effort should be made to eradicate them, as this is one of the forms of cancer whose adequate treatment is rewarded with a satisfying percentage of cure.

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KINESCOPE 11: CANCER OF THE ORAL CAVITY

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The purpose of this program is to emphasize the manifestations of oral cancer in order to promote earlier diagnosis and more prompt administration of adequate treatment. The role of the dentist in the recognition of oral cancer is discussed.

Differential diagnosis is presented through the use of a wide variety of illustrative material including benign as well as malignant lesions of the lip, tongue, cheek, palate, floor of mouth, and gingiva. The routes of lymphatic spread from these sites are diagrammatically shown. Principles of management of the primary tumor and its metastases are outlined in the modalities of surgery, electrocoagulation, and radiotherapy.

This kinescope is available through your Division of the American Cancer Society. Running time: 35 minutes; 16-mm. color with sound.

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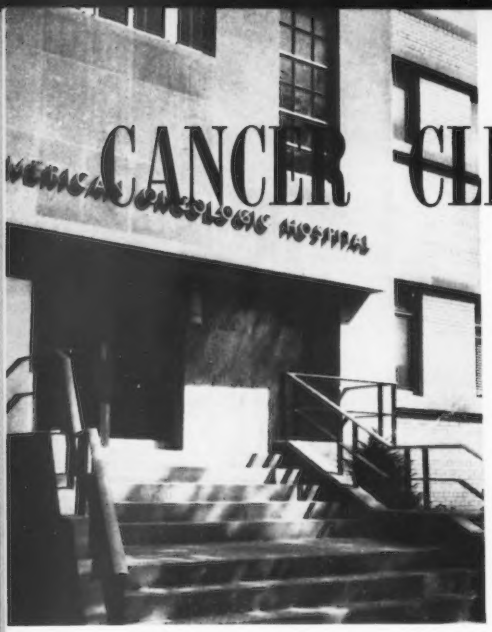
CANCER CLINICS



Tumor Conference from the Head and Neck Service, American Oncologic Hospital, Philadelphia, Pennsylvania

Synthesized by S. Gordon Castigliano, M.D.

The following case histories are actually synthesized from cases presented for my students in oncology on Friday mornings, during the operation of the head and neck clinic.

Inasmuch as transcripts of these informal presentations are not available, the dialogue in the following presentations is from memory.

DR. CASTIGLIANO: Before proceeding with the case histories that deal with and illustrate some of the problems encountered in oncology of the head and neck, a few general statements may be worth while.

Some of you may not appreciate the importance of malignant head and neck neoplasms. Many are surprised to learn that cancerous lesions of the head and neck make up from 15 to 20 per cent of all cancers.

Then, too, many of us do not realize how rapidly fatal mouth cancer is. At this point it should be mentioned that, when reference is made to mouth cancer, generally one speaks of epidermoid carcinoma, squamous-cell type. In fact, 90 per cent or more of all mouth cancer is squamous-cell carcinoma. Furthermore, probably 99 per cent of mouth-cancer deaths are attributable to this form of cancer.

Hence, we can see and appreciate that the real problem of mouth cancer is squamous-cell carcinoma. If squamous-cell carcinoma of the mouth did not exist, the remaining various types of cancers that occur in the mouth would in the aggregate constitute no serious problem. It is apparent therefore that, if significant improvement is to result in better survival rates for mouth cancer, it would be helpful to know something more of this disease and the diagnostic pitfalls that have befallen others.

One of the axioms of general cancer therapy is the importance of early diagnosis. That early diagnosis, and early adequate treatment no less, are vital to success in the management of oral cancer can be seen from a study of Fig. 1. This chart presents the survival rates of three different types of UNTREATED cancer. Thus we have a yardstick by which we can measure roughly the average time required for a given type of cancer to destroy life.

It is at once apparent that mouth cancer is at least as rapidly destructive of life as is cancer of the rectum, a well-known killer. The need for speed in diagnosis and treatment is apparent. The advice given by the first professional contact made by the patient may make the difference between life and death.

Case 1

B. H., a 65-year-old white man, was admitted to the Head and Neck Service of the American Oncologic Hospital (A.O.H.) on January 24, 1938, complaining of a "gum boil" of four and a half to five months' duration. About four months before admission the patient consulted a dentist. A loose tooth adjacent to the lesion in question was removed. Two months later, because the gum boil had broken down and ulcerated, two additional teeth were removed.

Since the ulcer continued to increase in size, the patient was referred to a physician, who administered local therapy for six weeks without improvement. The patient was then referred to the American Oncologic Hospital. The diagnosis of the referring physician was carcinoma of the gum.

Examination of the oral cavity on admission revealed a large, irregularly outlined, ulcerated lesion involving the left upper gingiva, with buccal and palatal extension. The over-all dimensions were 4×5 cm. The clinical impression was carcinoma.

A biopsy of the lesion was reported as necrosis, insufficient tissue for diagnosis. Despite this, and because of the strong clinical impression of carcinoma, the patient was started immediately on a course of irradiation therapy. (Neither the diagnosis of malignant neoplasm nor the treatment was given by the present staff.) Because the lesion failed to respond to this treatment, another biopsy was performed. The histopathological report was tuberculosis.

The patient was referred to a tuberculosis sanitarium.

STUDENT: Is oral tuberculosis frequently confused with oral cancer, as in this case?

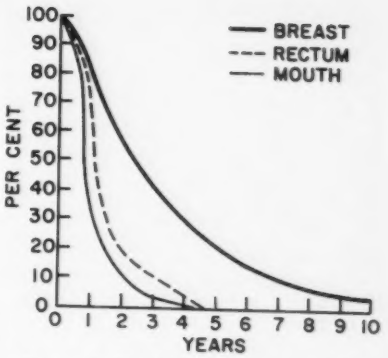


FIGURE 1. Survival rate for untreated cancer.

DR. CASTIGLIANO: The answer is "No!" In the first place, oral tuberculosis is rarely encountered except in tuberculosis sanitariums. At the A.O.H., during a period when about 2600 patients with oral epidermoid carcinoma were admitted, only eight cases of oral tuberculosis were seen.

Oral tuberculosis in general is essentially a disease of males, as is mouth cancer, but it appears in patients averaging ten years younger than the average patient with oral cancer. Occasionally a tuberculous ulcer may so closely simulate a carcinoma as to confuse the unwary clinician, as in this case.

RESIDENT: What is the prognosis in oral tuberculosis?

DR. CASTIGLIANO: The prognosis in oral tuberculosis is relatively poor, since it generally occurs in patients suffering with advanced stages of the pulmonary disease. On the other hand, it must be emphasized that an oral cancer in a patient with pulmonary tuberculosis may have a relatively good prognosis if the cancer is detected early and treated adequately.

It should be pointed out that probably one in every seventy-five to one hundred patients past 55 years of age with active tuberculosis could conceivably develop a carcinoma of the oral cavity, on a basis of percentages. Persistent oral ulcers in tuberculous patients should not be regarded

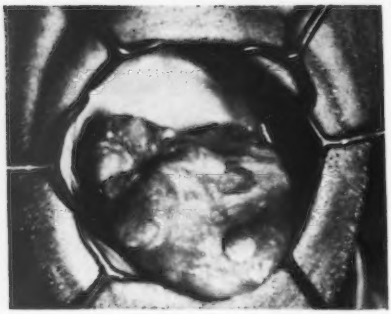


FIGURE 2. Far-advanced carcinoma involving the oral and pharyngeal tongue in a syphilitic patient. Note the leukoplakia, atrophy, and scarring, which represent the precursor lesions.

as being of tuberculous origin without microscopic diagnosis. To follow such a dilatory course would certainly condemn many patients with curable oral cancer.

Case 2

B. C., a 57-year-old white married man, entered the hospital because of a large ulcerating lesion involving the tongue. A mass presented in the left submaxillary region.

About eleven months previously the patient had consulted his family physician because of white patches and soreness of his tongue. His doctor gave him a liquid medicine to apply to the lesions. After three weeks the patient discontinued this treatment and consulted a second physician, who elicited a history of a penile chancre twenty-four years before. A serological test revealed a positive reaction. The patient was given intensive specific antiluetic therapy and was observed for several weeks without improvement. After this a pathologist was called in consultation, and a biopsy was recommended. Accordingly, a biopsy was performed and interpreted as leukoplakia, no evidence of tumor. The patient was referred back to the family physician, who administered various local treatments without improvement. Eleven months after the patient made his first professional contact, he was referred to the A.O.H. Head and Neck Clinic. Examination on admission revealed a tongue, including the base, frozen with cancer (Fig. 2). A fixed mass presented in the left side of the neck.

Tissue specimens were obtained from the tongue and cervical mass. They were interpreted as epidermoid carcinoma, squamous-cell type.

STUDENT: You did not mention the treatment.

DR. CASTIGLIANO: That is true. The treatment feature was not the reason for presenting this case. The patient improved under palliative roentgen-ray therapy but died about nine months after treatment.

The important feature of this case is professional delay in establishing a diagnosis at a time when the prospects for cure certainly were far better than when the patient was belatedly referred. Are there any questions with reference to this aspect of the case?

VISITING PHYSICIAN: Was the therapeutic test a justified or acceptable procedure?

DR. CASTIGLIANO: I would answer your question with an emphatic "No." The patient suffering from leukoplakia and suspected syphilitic glossitis, gumma, etc., should have an immediate biopsy—not therapeutic tests. Associated cancer must always be suspected at the outset in a patient who has signs of oral syphilis. It must be appreciated that the incidence of syphilis in patients with oral cancer is high —almost 30 per cent of tongue-cancer patients in this clinic have a positive Wassermann reaction (Table 1).

VISITING ORAL SURGEON: Is there any contraindication to the biopsy?

DR. CASTIGLIANO: It should be universally appreciated that in no condition with which oral cancer can be confused is speedy establishment of the correct diagnosis so vital to success as it is with oral cancer.

There is no contraindication to biopsy of oral lesions.

STUDENT: Can you explain why the first biopsy was negative?

DR. CASTIGLIANO: The appearance of epidermoid carcinoma of the mouth may be so strongly influenced by coexisting

syphilitic changes that the unwary or careless observer may fail to recognize the presence of carcinoma, apparently even when in an advanced stage.

In the presence of leukoplakia, syphilitic glossitis, gummatous scarring, etc., a single negative biopsy does not rule out cancer. Multiple biopsies are necessary before a negative report can be relied on. In this particular case the single negative and inadequate biopsy lulled all concerned into a false sense of security. It probably cost the patient his life.

The development of a deeper sense of guilt in our unwarranted failures would help as much as a major discovery in furthering the cause of cancer control.

Case 3

H. B., a 54-year-old white man complaining of a mass in the neck, was referred by the Chief of the Oral Surgery Department of a large community general hospital.

The referring oral surgeon stated that the patient had been first seen in general surgery and was referred to oral surgery with a diagnosis of cervical abscess secondary to dental infection. In the Oral Surgery Department the patient was treated with penicillin. The mass in the neck was incised on three occasions during a period of two months. After more than three months of intermittent treatment, a biopsy was obtained. The pathological report was metastatic squamous-cell carcinoma. Three weeks later the patient was referred to the Head and Neck Clinic.

TABLE 1

Incidence of Positive Wassermann Reaction in Oral Malignant Disease

(American Oncologic Hospital)

Site	%
Tongue	29
Buccal surface	14
Lip	9
Gum	7
Floor	6

FIGURE 3. Draining, fixed mass of metastatic nodes involving the left midmandibular and submaxillary areas. Note that the primary lesion, which involves the lip, is scarcely visible in this view. The mass in the neck was mistakenly diagnosed as a cervical abscess prior to belated referral.

The examination revealed an infected, draining, infiltrating, fixed mass about 7 cm. in diameter in the left submaxillary area (Fig. 3). A previously unrecognized small, scaling, plaquelike lesion of the vermilion zone of the lower lip was found. A biopsy of this small lesion was reported as squamous-cell carcinoma. Complete examination failed to reveal another primary lesion.

RESIDENT: Why was a clinical diagnosis of abscess made of this neck mass?

DR. CASTIGLIANO: Of course, I cannot speak for those who first saw the patient. It may be mentioned that masses in the neck are most commonly the result of infection. Nonetheless, it is a grave responsibility that one assumes in accepting the care of a patient with a lump in the neck. Malignant disease must always be thought of and excluded. Unfortunately, in this particular case a small primary lesion was missed by all concerned in the earlier management of a case already advanced by patient neglect.

STUDENT: Do such small cancers usually produce such large metastatic masses?

DR. CASTIGLIANO: Generally, no. However, massive metastasis from small lesions is by no means rare. Early large metastases from small lesions notoriously develop from certain head and neck sites.

For example, it is not rare to find massive metastasis from a minute primary malignant neoplasm in the pyriform sinus, the nasopharynx, and, less commonly, even the tonsil and tongue, or, as in this case, but rarely, the lip. It should be emphasized that a lump in the neck may be the first and presenting complaint of a patient with head and neck cancer.

DR. SKIGEOKA: Could the mass in the neck be independent of the small labial lesion? I'm thinking of the possibility of a malignant change in a branchial-cleft cyst.

DR. CASTIGLIANO: One could not deny the possibility, but as you know branchial-cyst cancer is rare. No microscopic supportive evidence to bend one toward such a diagnosis exists in this case. My personal belief is that carcinoma arising in a branchial-cleft cyst should be diagnosed only when no other diagnosis can explain the findings. Even in such cases one must delay long enough to allow the development and clinical recognition of an occult primary lesion. In some rare cases three or more years elapse before the primary lesion is discovered. In other cases the small and occult primary lesion may be destroyed by the same treatment that may control the metastasis.

In closing, I should like to point out that in this case, again, we have an example of professional delay in instituting proper therapy because of delay in obtaining an adequate biopsy. We must learn that the biopsy should be done early. Even in a case such as this, which appeared to be an abscess to the first observers, the wall should be biopsied during the procedure of incision and drainage.

It is fallacious to regard the biopsy as a procedure to consider only when a given case does not appear to evolve normally. Early, accurate, and conclusive diagnosis is of supreme importance, as the patient's life hinges upon it if the diagnosis is cancer.

Medical educators have not yet achieved unity of thought concerning the supreme importance of avoiding delay in ruling out malignancy of suspected lesions in the various body areas. On the one hand, zealous, resourceful, and articulate workers have achieved a remarkably standardized and decisive approach to the early recognition of cancer in some body areas; on the other hand, in other body areas much is left to be done before comparable progress is made. Oral malignant disease belongs in the latter group.

KINESCOPE 12: CANCER OF THE THYROID

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The subject is introduced by a classification of the types of thyroid cancer and by a statement of the incidence of this disease in the young and old. The current status of surgery, radiation, and radioactive-iodine therapy is presented in relation to localized, regional, and distant disease.

This kinescope is available through your Division of the American Cancer Society. Running time: 29 minutes; 16-mm. color with sound.

APPROVED FOR INFORMAL STUDY CREDIT BY THE
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S' DILEMMAS

Q *Three months ago, my patient, a woman of 37 years, developed severe and intractable neck and head pain that required large amounts of opiates for control. Results of careful studies, including skull and sinus roentgenograms, an electroencephalogram, and a spinal tap, were all within normal limits. She was advised by another physician to see a psychiatrist but demurred. An eye, ear, nose, and throat consultant and a neurologist have seen her. Her pain continues unabated—and unexplained. Three weeks ago a rather diffuse swelling was noted in the posterior cervical triangle. Aspiration biopsy showed anaplastic carcinoma. Careful reexamination, including biopsies of the nasopharynx, failed to reveal any primary lesion. How can I relieve this patient of her pain and best manage her disease from the long-term point of view?*

A Although the disease is uncommon in women, and despite the fact that the several biopsies from the nasopharynx failed to reveal any evidence of a primary lesion and that careful search for the primary source of this patient's cancer has been unrewarding, it is extremely likely that the patient has a lymphoepithelioma of the nasopharynx, a most difficult part of the body to visualize. Treatment might include the administration of nitrogen mustard, because of the anaplastic nature of the disease, and irradiation through two portals over the maxillary areas, angled toward the nasopharynx and base of the brain, totalling not less than 3000 r in air to each area. It is often possible to control such a clinical picture for months. Surgery has no role in the management of such a problem as described.

Q *A 13-year-old high-school boy injured his knee during a basketball game about seven weeks ago. On physical examination at that time there was redness, swelling, and pain, with some limitation of motion. In spite of rest and antibiotic therapy, there has been little improvement. In fact, the swelling has increased slightly. What further investigation is indicated.*

A Frequently, minor trauma will call attention to a pre-existing bone tumor. Although this boy may have nothing more serious than a simple injury, roentgenograms for bone detail should be taken without further delay, to rule out the presence of bone tumor or osteomyelitis that is not responding to the antibiotic therapy.

Q *A 32-year-old policeman came to the office last week with a history of a progressively enlarging swelling on the inner aspect of the middle third of the left thigh, of about two months' duration. There has never been any pain, limitation of motion, or definite history of injury, but, because of the red appearance of the area and the fact that he is on his feet so much, I am inclined to think that he may have a hema-*

toma within the muscles of the thigh, incurred without his being aware of any specific trauma.

A Your appraisal of the situation may indeed be correct. However, the patient's lesion is in a very common location for sarcoma of the soft tissues. It would seem that a formal biopsy of the involved area should be done, which perhaps might establish an early diagnosis of a malignant tumor. Roentgenograms of the femur should be obtained, to see if there is the characteristic periosteal reaction often associated with soft-tissue sarcomas.

Q *A 43-year-old white woman had a radical mastectomy two years ago and now has extensive bone metastases. For the past four months she has been receiving injections of testosterone with no apparent improvement. More recently she has had severe attacks of nausea and vomiting, associated with marked weakness. Roentgenograms of the gastrointestinal tract show no intrinsic abnormalities. What further studies should be done?*

A It is quite probable that this patient is suffering from hypercalcemia, secondary to mobilization of calcium from the involved bones into the circulation. A blood-calcium determination will establish or rule out this possibility immediately. If the calcium is elevated, this patient should be placed on a low calcium diet and high fluid intake. The study of blood potassium and chloride is also indicated (in view of the episodes of nausea and vomiting) to determine the need for replacement therapy with potassium and chlorides. This case appears to represent a failure of testosterone therapy. Perhaps an empirical trial of estrogen therapy would be worth while for the patient at this point.

Q *I have a patient, 34 years old, who developed carcinoma of the cervix, classified Grade 2, six months ago. She was treated by irradiation. There is now no local evidence of disease. During the past two months, however, she has developed bone metastases and opthalmoplegia of the left eye. Can these metastases be due to cancer of the cervix?*

A If these metastases represent a spread from the cancer of the cervix, the case would be one of the few to be documented. It is more probable that this patient has developed another cancer the primary site of which is not yet evident. In this age group, metastases of the type described are most commonly found to be from cancer of the breast, thyroid, or kidney.

Q *I have recently heard that the incidence of cancer is considerably greater in diabetics as compared with the general population. Is this correct?*

A Yes. Studies by Joslin and others report a significant increase in the incidence of cancer among diabetics. Elsewhere it has been reliably reported that the risk of cancer may be as much as eight times greater among diabetics than in the nondiabetic population.

A routine medical examination of the mouth is far too often hasty. The average examination consists of asking the patient to open the mouth and say "ah." About all that is accomplished thus is a cursory glance at the surface of the tongue, occasionally the inside of the cheeks and the palate, and perhaps a slight glimpse of the tonsils. Many tumors are not recognized by such superficial inspection.

Ward, G. E., and Hendrick, J. W.: Diagnosis and Treatment of Tumors of the Head and Neck, Baltimore. Williams & Wilkins Co. 1950.

new developments in cancer

Amino Acid Metabolism . . .

After failing to detect any abnormal pattern of amino acids in tumor-bearing animals, David M. Greenberg and E. Norberg Sassenrath of the University of California wondered whether normal and tumor-bearing animals might metabolize amino acids differently. They injected rats intraperitoneally with massive doses of several amino acids. They found in tumor-bearing rats a significant change in the concentration of injected glycine, serine, threonine, and proline, and other metabolically interrelated amino acids. Glycine, particularly, was metabolized very rapidly by tumor-bearing animals, and an altered threonine dehydrase level in the liver (serine dehydrase was unchanged) indicated that enzyme levels might offer a sensitive assay of amino acid–metabolism derangements.

Aldolase in Tumors . . .

Aldolase, indispensible in carbohydrate metabolism, has been thought by some to be the limiting enzyme in tumor glycolysis. Serum-aldolase levels have been found high in some rat and human cancers. John A. Sibley and Gerard A. Fleisher of the Mayo Clinic have found more aldolase in the malignant tissue of twenty-three surgical specimens of adenocarcinoma of the colon and rectum than in adjacent normal tissue. Now they will try to determine whether there is a corresponding decrease in oxidative enzymes to represent the radical shift in metabolic methods of meeting tumor energy requirements.

Nodular Goiter . . .

The knotty questions of whether nodular goiter may become malignant and when to operate have been put on a statistical basis by Joseph E. Sokal of the Roswell Park Memorial Institute. Sokal reasons this way: Of 10,000 people, eleven will develop thyroid cancer at some time, eight of them in pre-existing goiter; but 1000 will have nodular goiter at some time during their lives. Therefore: The cumulative lifetime risk of cancer in nodular goiter is 8:1000, or 0.8 per cent. He seriously questions the advisibility of routine thyroidectomy for nontoxic nodular goiter and contends that it is possible to differentiate with considerable accuracy between benign and potentially malignant conditions.

Quinacrine Treatment . . .

Acridine derivatives, including that familiar antimalarial atabrine, are showing

considerable promise in animal experiments as potential anticancer agents. These were used in 1948 by M. R. Lewis and P. P. Goland of the Wistar Institute against mouse sarcomas and carcinomas. Of the seventy derivatives tested, sixteen 9-aminoacridines restricted the growth of tumors in treated animals to one twentieth or one fortieth of the size of tumors in untreated controls. Treatment was for fourteen days. John W. Vassey and others at the University of North Carolina did not obtain the dramatic results with atabrine (also called quinacrine) reported by Lewis and Goland, but they did note a one-third to one-half decrease in the growth rate of a mouse fibrosarcoma, granulosa-cell tumor and carcinoma. The treatment lengthened lives a little beyond those of controls, increased slightly the number of recoveries from carcinoma, and appreciably decreased the external necrosis of tumors. Treated immature animals stopped growing. The quinacrine concentrated, in descending order, in liver, pituitary, adrenal, spleen, kidney, lung, thymus, pancreas, heart, tumor, testis, blood, and brain. Carl Tabb Bahner at the Oak Ridge Institute of Nuclear Studies, in testing compounds related to 4-(*p*-dimethylaminostyryl) quinoline methiodide, found evidence that the antitumor effect of the drug was different from the antibacterial effect. For one thing, the presence of the iodide ion was not essential for antitumor activity. Oral administration was much more effective than subcutaneous or intratumoral injections.

Cancer and Diabetes . . .

Scientists at the University of British Columbia have reported a curious antagonism between induced diabetes and some forms of cancer in rats. E. S. Goranson and G. J. Tilser found that when they gave rats diabetogenic doses of alloxan before or after intraperitoneal implants of a certain hepatoma or carcinoma, the size and growth rate of the tumor were reduced. The reduction was inversely proportional to the severity of the diabetes. In like manner, tumors implanted intraperitoneally before or after alloxan administration reduced the drug's diabetogenic action. These results could not be obtained when tumors were transplanted subcutaneously. Histological studies indicated that the tumors somehow protected or stimulated beta cells of the pancreatic islets.

Nonlethal Prostatic Cancer . . .

Hugh B. Jewett of Johns Hopkins Hospital has found that about one half of all men treated for early prostatic cancers live out a normal life span. A review of 357 radical prostatectomies performed over the last fifty years showed that 49 per cent of the patients lived ten years or longer. Fifty-three per cent of men of the same age in the general population lived ten years or longer. The findings have convinced Hopkins investigators that early detection (by a one-minute routine digital examination) and prompt treatment are lifesaving. These measures would save many of the estimated three million American men who today have prostatic cancers — either recognized or undetected.

Hirsute Viruses . . .

The viruses that infect sewage bacteria have long hairlike structures on their "tails." This finding, by Robley C. Williams and Dean Fraser of the University of California, has inspired speculation that the "hairs" may supply the physical (electrostatic) or chemical (enzymatic) means by which the viruses first attach themselves to cells. The scientists have also observed in their electron microscopes that the virus "tails" contain an inner core or plug that, when removed, enables the virus to inject its nucleic acid into the cell victim. The plug, probably protein, also may enter the cell and supply the enzymatic activity necessary to transform the cell into a virus factory.

to be on a very lavish scale, and parts of it would almost certainly require international co-operation.

Russell (Oak Ridge) has found that the mouse induced-mutation rate is fifteen times higher than the drosophila mutation rate. From a scientific point of view, it would be unwise to generalize. However, since we are concerned with the immediate practical problems of protection in man, it would be risky to ignore the indication that calculations of human hazards based on drosophila mutation rates may seriously underestimate the damage. Analysis of the data on spermatagonia of the mouse shows no significant change in mutation rates with time after irradiation. It may be concluded that these data indicate that, in man, offspring conceived long after exposure of the father to radiation are just as likely to inherit induced mutations as those conceived a few weeks after exposure. Although postponement of procreation for a few weeks after exposure would reduce the total risk of transmission of mutational changes, by excluding these induced spermatogonial-stage changes, further postponement would not give any additional reduction in risk.

Carling (Home Office, England) raised the question: If all mutations are deleterious, how is it that the race has survived through the age-long course of evolution? It would seem that the 0.5 per cent or even 0.1 per cent of beneficial mutations grudgingly allowed by geneticists had been extremely potent. Is there not some stabilizing factor operative over many generations? Among the 15,000 or so human genes, what are the mathematical chances that in the course of a lifetime or in the course of ages, a "bad" gene may suffer a change of benefit to the individual or race? The gene that transmits liability to sickle-cell anemia seems to confer immunity to a form of malaria. In a world contemplating a future in which the expansion of its population may outrange its food supply, it is conceivable that diminished fertility and shortening of the life span might not be altogether to be deplored. However, since a diminution of general intelligence might result, speculation is depressing, but it is to be hoped there may still be 'sports' of extremely high intelligence who would suffice to leaven the lump.

To the nongeneticist, it appears that for the benefit of the race as a whole in the future, one mutation that results in an Aristotle, a Leonardo, a Newton, a Gauss, a

Pasteur, or an Einstein might well outweigh ninety-nine that led to mental defectives.

Atomic Energy Commission; press release at Atoms for Peace Congress. The atomic-energy industry is one of the safest industries in the United States, according to records of the National Safety Council. The Safety Council's award of honor was presented to the Atomic Energy Commission in 1953. Less than 2 per cent of the injuries experienced to date in the atomic-energy field have involved radiation as a factor.

Anticancer Drugs and Longevity: Shimkin (National Cancer Institute) told the Congress that drugs developed during the last thirty-nine years have not added to the life span of patients with lymphatic and blood cancers. He based his observation on a comparison of 221 patients treated during 1948-1953 at his San Francisco Laboratory of Experimental Oncology with other cases seen at the University of California Hospital between 1915 and 1947. He reported that the mean duration of disease had not been altered appreciably during the thirty-five-year period or by the more recent chemotherapeutic additions. Drugs tested and found wanting, so far as increased longevity is concerned, included three nitrogen mustards, TEM, myleran, urethane, Fowler's solution, stilbamidine, pentamidine, cortisone, ACTH, aminopterin, amethopterin, and combined antibiotics; also induced and spontaneous infections, and miscellaneous agents, gave negative results.

Research Advances in Germany: Druckrey (Freiburg), besides reporting his own experiments indicating the irreversible nature of carcinogens and an indirect ratio between dosage and disease latency, cited other work that indicates that the microsomes play an important role in carcinogenesis. Friedrich-Freksa and Weiler (Tuebingen) have succeeded in developing organ-specific antibodies. Coupled with fluorescein, these marked antibodies were traced and, moreover, they were traced to microsome fractions. As cancer developed in liver cells of rats (fed carcinogens), the cells progressively lost their organ-specific antigenic qualities. Dye-tagged antibodies bound by normal liver cells were less and less bound by liver cells undergoing carcinogenesis. These results have led the investigators and Druckrey to conclude that the primary effect of carcinogenic action is to be found not in the nucleus but in the cytoplasm.

COMING MEDICAL MEETINGS

Date 1956	Meeting	City	Place
Feb. 4-10	Mid-South Postgraduate Medical Assembly	Memphis, Tenn.	Hotel Peabody
Feb. 5-8	Chicago Dental Society	Chicago	Conrad Hilton Hotel
Feb. 10-11	American College of Radiology	Chicago	Drake Hotel
Feb. 20-21	Tri-State Medical Association of Carolinas-Virginia	Charlotte, N. C.	
Feb. 28-March 2	Chicago Medical Society	Chicago	Palmer House
March 12-16	Southeastern Surgical Congress	Richmond, Va.	John Marshall Hotel
March 19-22	American Academy of General Practice	Washington, D. C.	D. C. National Guard Armory
March 22-23	Mid-west Cancer Conference	Wichita, Kansas	Broadview Hotel
April 8-13	John A. Andrew Clinical Society	Tuskegee, Alabama	John A. Andrew Memorial Hospital
April 9-11	American Radium Society	Houston, Texas	Hotel Shamrock
April 10-12	American Association of Railway Surgeons	Chicago	Drake Hotel
April 12-15	American Association for Cancer Research	Atlantic City	Chalfonte-Haddon Hall
April 16-18	Aero Medical Association	Chicago	Drake Hotel
April 16-20	American College of Physicians	Los Angeles	Shrine Auditorium
April 16-20	Federation of American Societies for Experimental Biology	Atlantic City	Auditorium
April 23-26	Industrial Medical Association	Philadelphia	Convention Hall
April 24-25	International Academy of Pathology	Cincinnati, Ohio	
May 14-18	American Nurses' Association	Chicago	Conrad Hilton Hotel
May 20-25	National Tuberculosis Association	New York	Hotel Statler
May 23-25	Upper Midwest Hospital Conference	Minneapolis, Minn.	Municipal Auditorium
May 28-31	American Urological Association	Boston	Hotel Statler
June 4-6	Third National Cancer Conference cosponsored by National Cancer Institute and American Cancer Society, Inc.	Detroit, Michigan	Sheraton-Cadillac Hotel
June 6-9	American Proctologic Society	Detroit	Hotel Statler
June 7-9	The Endocrine Society	Chicago	Palmer House
June 7-10	American College of Chest Physicians	Chicago	Hotel Sherman
June 10-14	Canadian Medical Association	Quebec, P.Q., Canada	Laval University
June 11-15	American Medical Association	Chicago	Navy Pier
June 17-22	American Society of Medical Technologists, Canadian Society of Laboratory Technologists, Joint Session	Quebec, P.Q., Canada	Hotel Frontenac

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Cancer Registries

As of January 1, 1956, operation of a cancer registry became a minimum requirement—in addition to (1) a Committee on Cancer and (2) a Cancer Consultation Service or a Cancer Consultation and Treatment Service—for survey, by the American College of Surgeons, of cancer programs in general and special hospitals conducting cancer clinics and cancer diagnostic clinics. Details of organization and operational procedures for a satisfactory cancer registry have been worked out by the Committee on Cancer of the American College of Surgeons and are published as a Manual for Registries and Cancer Clinical Activities by the Department of Professional Services and Accreditation, American College of Surgeons, 40 East Erie St., Chicago 11, Illinois, at 50 cents per copy. This twenty-page brochure contains pattern blanks for recording pertinent data, a Cancer Registry Abstract, a Year Book (Accession Register), and a Patient Index Card.*

A cancer registry, to be accredited by the Committee on Cancer, American College of Surgeons, must contain the record of every cancer patient, private and public, in-patient and out-patient, admitted to the hospital. It includes a standardized abstract of each patient's clinical record and annual follow-up notes.

Operation of cancer registries should be extended beyond the special cancer institutions to include all facilities concerned with diagnosis or treatment of cancer and with the statistical study of cancer, at county, state, and national levels. When this has been accomplished, workers in this field will have reliable statistical information upon which to base further research and improvements in the diagnosis, treatment, prognosis, and control of cancer.

**Forms acceptable for use in accredited Cancer Registries are commercially available in quantity from Medical Case History Bureau, 17 West 60th Street, New York 23, New York.*